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Approaches to Feeding Control

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Abstract. This overview is mainly a comparison of various theoretical and experimental approaches to the investigation of feeding control mechanisms, although some suggestions are made on the practical problem of gaining control of feeding. Verbal and computable theories are contrasted, and fragmentary explanations put alongside unified system explanations. The psychology and physiology of appetite in the omnivore rat is taken as a primitive model for internal and external controls of human feeding. It is emphasised that all areas of appetite science, from brain research to learning theory, must construct mechanistic hypotheses of the processing underlying the phenomena if the science is to advance further. A computerised whole-system theory of food intake control in the rat is summarised, which accounts for appetite with a combination of an energy-flow receptor system and learning about feeding and its effects. The model is a source of questions for experimentation in man. It implies that the brain rules appetite largely through gastroduodenal control of absorption rate.

INTRODUCTION

> "The test of any analysis is synthesis...If we truly understand the nature of the control of food intake, then...we should be able to predict quantitatively the amount we will eat in any given set of circumstances." (Teitelbaum, p. 327)

This Conference was organised around a division of appetite science into four areas. That meant a uniquely wide and balanced representation of the relevant disciplines. Before the control of appetite can be specified precisely and realistically enough to produce a predictive theory of the causes of food intake, a systematic view of the processes

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underlying feeding has to be developed. Theoretical positions have to be taken, right or wrong, in each of the four areas of appetite research. This overview was written in an attempt to communicate the beginnings of such a conspectus, ranging from brain research to clinical interests and pointing to an integration of peripheral physiology and cognitive psychology in the explanation of appetite. The integration is of course sketchy and highly selective, paradigmatic as well as concrete, critical as well as constructive, and far from an all-inclusive review. The reader of other chapters in this book can gain some impression how acceptable the themes of this chapter were within the different groups. The pre-Conference version has been clarified and corrected in places in the light of discussion at the Conference. Nevertheless, this remains a personal viewpoint, not a statement with which other members of the Conference may be taken to have agreed.

The central theme of this overview is abstract but simple and was implied in the third sentence. Genuine explanation in science is the invocation of processes which are in or behind the phenomena to be understood or predicted. Implication of a structure in feeding control only raises the question what is going on there. Implicating a substance simply poses the question what it does. With answers we might gain a rationale for using the anatomical or chemical information.

BASIC PSYCHOLOGICAL ANALYSIS

When a person or an animal is hungry or has an appetite, he wants food or has the urge to feed. In ordinary English, all four ways of speaking have the same meaning. This concept of the desire for food is eminently suitable for scientific use, because it is objective and is descriptive, i.e. relatively free of explanatory baggage. Unfortunately, the terms "hunger" and "appetite" are persistently redefined and the redefinitions disagree. This is often because the psychological formulae the definers are trying to rescue also disagree. Also, the original meaning is very simple and it is fairly arbitrary to draw distinctions within the phenomena

by reserving one word for one phenomenon. For example, if "hunger" is used to refer to the sensations habitually experienced when appetite is strong, then the safe term is "hunger sensations". My 7-year old said just before a meal: "I really am hungry". I asked him if he meant he had feelings in his midriff or somewhere and he replied "No, I want something to eat".

The words are a "chapter heading" reference to a motivational state - the mental attitude or the behavioural propensity of wanting food to consume: that is, the tendency to seek and to take material which is believed to be nutritive. The desire for food is a relation with two terms - the subject and the food. Differences between foods, taken against some assumed state of the subject, are incentive variables or, in ordinary language, palatability. Differences between states of a subject, implicitly with respect to some food presentation condition, are degrees or types of hunger/appetite or satiety. When someone is satiated, he lacks the desire for food because of recent feeding. It is convenient to use the term anorexia for loss of hunger from other causes.

Motivation is a structure in behaviour - an aspect of its current control characteristics. It is not a (quasi-) physical cause of behaviour, like the tug of a string or the pressure of a head of water, for behaviour is not like a block of wood - especially not a block of wood as viewed by the physics of Aristotle, rather than that of Newton (in which motion needs no explanation). We should not have deserted the paradigm (91) of motivation as the selection among ongoing activities (including alert immobility and sleep) for the reflexological behaviorism which needs a 'Go' mechanism and then still has to explain where the organism goes. The division of the causes of food-oriented behaviour into external and internal pushes or pulls, to accord with that paradigm, cannot cope with the experimental evidence for multiple connections between food and body stimuli. One advantage of systems models is that they bypass the rigid distinctions arising from a linear view of cause and effect

and show that view up as another misleading halftruth transferred from schoolboy physics.

The psychology of feeding has suffered from psychologists' preoccupation with experimental paradigms invented to serve general learning theory. There are major motivational phenomena in food intake control which must soon be systematically investigated at the purely behavioural level. Here are two ancient examples.

Motivational effect of need

With the partial exception of nutrient-specific appetites alluded to later, the relation between palatability and nutrient deficit is remarkable for the contrast between the vigour with which it is expounded and the paucity of data and experimental design.

The simple examination of the way that taking a meal reduces the pleasantness of the odours specifically of ordinary foodstuffs (47) needs extension to relate the pleasantness ratings to other major psychophysical, verbal and experiential aspects of appetite, and to intake or food-search changes. What does a hunger or satiety rating convey about current attitudes to specific foods or about specific oral or visceral sensations? The mediating processes in the loss of appetite need to be characterised: how much is sensory adaptation, and how much is a shift in reactivity to stimuli which (somehow!) share a significance as food?

Le Magnen (99) has an experiment with rats whose food is made tasty with oil or revolting with cellulose, in which a facilitatory effect of food deprivation on initial intake is augmented for the oily food (eaten fastest in any case). This palatability manipulation is nutrient-confounded and fairly extreme. Yet the more common experiment has been to vary the concentration of saccharin or sucrose in water, which may have nothing to do with the interaction between my energy need and what's to eat for breakfast.

From even more extreme manipulations, Jacobs (82) has suggested that organisms are controlled by taste when hungry

and by calories when freely fed. A reexamination of the phenomena has provoked a less paradoxical suggestion (14), purpose-built for systematic investigation: pleasant flavours become more pleasant, but unpleasant flavours less unpleasant in hunger relative to satiety.

The stimulating effect of variety

The rat shows olfactory alternation (72) and hyperphagia when faced with choice (97) or repeated change of food odour (93) or even just its intensity (94). We all regard variety as a most important spice in our meals: a single foodstuff soon palls. Possibly, sheer lack of interest is as important as abnormal caloric dilution and poor palatability in the power of feeding exclusively on Metrecal to overwhelm caloric intake stability even in lean subjects (171).

Once again, students of (animal) behaviour processes have shown a profound lack of interest in analysing a major determinant of normal food intake. Le Magnen (93) suggested that the hyperphagia was an effect of conditioned satiety, but it is not clear how such an explanation applies. Dishabituation is a possible mechanism: an abrupt external stimulus such as a noise, pinch or needle stab, so long as it is not too aversive or persistently distracting (40), may elicit feeding in the fed rat (3, 23, 46), and even obesity (145). The results of month-long familiarisation with test odours (93), shown in Table 1, suggest that the facilitation produced by a change of food-odour depends on non-associative effects of extensive familiarisation with the first odour but are independent of prior exposure to the second odour.

TABLE 1 - Food intake (g in 30 min) after a change in odour (19)

First odour	Second odour		
	(a)	(b)	(c)
Unfamiliarised (a)	2.0	2.5	2.3
Familiarised with food present (b)	5.5	4.9	3.8
Familiarised in absence of food (c)	5.1	5.0	4.9

Attenuation of the effect of nonspecific stimuli on specific sensorimotor reactions (such as those of ingestion) is a major component of lateral hypothalamic aphagia (190). Such phasic effects of environmental disturbance are represented in our computer model of feeding control (see below).

TEMPORAL PATTERN IN FOOD INTAKE

Stochastic analysis of feeding behaviour is an important descriptive tool (e.g. Metz, Heiligenberg, Lloyd (111)) which at least puts limits on theorising about underlying control mechanisms, even if it cannot establish hypotheses as to control processes. The conditional probabilities of transitions between non-feeding behaviour and mouthful-sized units of feeding behaviour, and related survivorship plots of mouthful-to-mouthful intervals, point to mechanisms such as locking into feeding at the start of a meal, growth and decay of satiation, circadian variations, and interaction with other motivation. Meals in man (unfortunately on abnormal liquid diets) (2), insulin effects in the rat (17, 29) and oestrus cycles in mice (133) have been examined in this way. System theories of sensorimotor control in motivated behaviour are required to put such data to full use. They are also needed to analyse and to interpret data on frequencies and durations of bites in human meals, reported and reviewed by Hill (69).

System theories do now exist which begin to cope with analyses of the longer-term patterns of meals and intervals between them (e.g. 102, 131). The abstract Geertsema models (55, 56) and the more physiologically based Booth-Toates-Platt models (22, 34, 35, 180) predict qualitatively and statistically meal-pattern data in the typically reported form of means and standard deviations by day and night. Unfortunately a mathematical theory soon poses data questions that such reports do not answer: one man's statistical summary poisons another man's re-analysis (152) - an argument for not letting mathematical data analysis get ahead of mathematical theoretical explanation.

These mathematical models reduce meal sizes and meal-to-meal intervals to epiphenomena of interactions between continuous facilitatory and inhibitory influences. Talk about separate control of meal size and meal-to-meal interval, or of the stopping and starting of eating, may therefore be an unfortunate hypostasis.

Le Magnen and Tallon (102) contrasted the correlation between meal size and succeeding interval with lack of correlation between prior interval and meal size in the freely fed rat. Subsequent controversy has elucidated that such correlations must be based on individual meals and calculated over segments of the 24 hr in which meal patterns are fairly stable. With the help also of their later paper (103) on deprived animals, at least one reader realised that the inhibitory after-effect of feeding had a far greater influence on food intake than any facilitatory effects of imposed deprivation, and promptly stopped looking for "hunger signals" to search instead for normal satiety mechanisms. Some may still doubt the distinction. Ultimately it will turn on the dynamic range of the appetite/satiety receptor system.

Motivational state-space analysis

McFarland and associates have pursued an important line of purely behavioural modelling in the ethological tradition. This provides a common currency for trading off appetite against other motivation with which it has to compromise. The theory has now been axiomatised (113). Accepting the difficulties of behavioural variability and limitations on convenient manipulation of candidate motivations, behavioural experimentation can define a space of motivational states with lines at which behaviour switches from, say, eating to drinking (or, in principle, from talking to eating, or from having a meal to typing a paper to deadline).

One finding is that candidate motivations do not compete directly but time-share, with a subdominant behaviour occurring but being more susceptible to alternation to the dominant behaviour, after an interruption for example (112).

This idea creates some interesting alternative explanations of the meal-taking behaviour which man and rat both have: they often end the meal with drinking, they begin it with less substantial drinking, and, quite often, they take little or nothing during the main feeding bouts. Is this interrelation of feeding and drinking during meals largely a matter of time-sharing between dominant and subdominant behaviour? Alternatively, does it reflect the instantaneous intensities of current or anticipated physiological processes such as energy and water absorption? Or, different again, is there innate or acquired sequencing in behaviour? That is, as the old joke has it, our hypothalamus makes us eat, drink, love and sleep - preferably in that order.

Another major problem in the theory of motivational interactions is to explain the usual bistable characteristic of a switch in behaviour: once a meal starts, it rapidly becomes highly likely to continue. McFarland (110) and Wiepkema (188) adduced positive feedback on feeding from the effects of feeding, although the fact that preparations without negative feedback do eventually satiate unless they have been starved beforehand (163) creates a problem for simple versions of this view (Toates (179), p. 241). A neural network model for appetite and satiety incorporates the flipflop property in hypothalamic processing (6).

Geertsema's (55) and our feeding models and the Toates and Oatley (181) drinking model use an alternative theory, of two thresholds, one to turn ingestion on and a higher one to turn it off, i.e. hysteresis. In our current computer model (22), this may reduce to a third concept which McFarland and Sibley (115) cite: the route to the switching value may determine the consequence of being there. Much biological development into stable dynamic states can be impressively well characterised in Thom's "catastrophe" mathematics (196). The relative costs and benefit of feeding and alternate activities can constrain the point at

which the organism flips into or out of feeding as much as the factors controlling feeding itself (155).

Whatever the decision control processes are, they will have to be represented in combination with peripheral physiological processes before fully realistic models become available ((179), p. 240). Furthermore, the input-output specification will probably have to be this explicit before neurophysiological experiments can be designed whose results might be useable to build realistic theories of the processing in brain systems affecting appetite. Stimulus processing and motor processing will not meet in the middle. Recognition is not mere sensory inflow, acts and reactions (like even reflexes) are not mere motor outflow, and motivational decision is not simply a matter of stimulus competition and/or response competition (113).

LEARNING IN INTAKE CONTROL

The human infant, much like the rat, has some innate oral sensorimotor reactions (rooting, suckling, facilitation of suckling by fluid delivery and by sweetness) and an innate distress pattern during water and energy need. But these do not constitute a desire for food. The propensity to consume materials which are nutritious, as well as the propensity to seek them, is probably a mixed involuntary and voluntary activity (like almost every human behaviour) which has compromised between need and other influences by habituation, conditioning and instrumental learning to come under the control of visual, oropharyngeal and visceral sensations.

Oatley (126, 127) has cogently argued that motivational systems theory of both appetitive and consummatory behaviour will have to include more than homeostasis and decisions between homeostatic behaviours. Animal as well as human motivation includes representations of the environment (of which, he likes to say, a systems theory is itself an example). In appetite, and probably in all behaviour, the environment represented is internal as well as the more richly sensed external. Furthermore, the representation of contingencies generates motivational significance (8, 12).

Motivation-specific "drive" effects of deprivation and "reinforcement" effects of feeding are often treated as primary or innate but the importance of learned representations in the motivating roles of external and internal stimuli must not be underrated, as Bruch (38) has emphasised. Indeed, it is a matter of logical principle that hunger sensations and satiety sensations can be identified as such only by their concomitance with the objective desire for food and its dissipation by feeding (see Wittgenstein's (189) refutation of private language).

There is, on current knowledge, the possibility that acquisition of the discriminative and motivational aspects of both hunger and satiety sensations, and the sensations generated externally by the approach to and ingestion of food, is based on the operation of a single interface between the body and the nervous system. This interface system may respond to consequences of energy flow to lean tissue (see our model below). Operation of the interface need not be accessible to awareness - the old controversy between local and "general" sensations is an unnecessary muddle.

Visceral stimuli

There is little or no evidence that the abdominal sensations of normal repletion are mediated by gastric or intestinal stretch, and the evidence that hunger pangs depend on gastric or intestinal motility is not particularly strong (83). Innately, gastrointestinal distension may only be a safety mechanism providing pain and distress if pathologically large gastric or intestinal intakes occur; in our model it plays a negligible role in normal meals. Mechanoreceptors in the peritoneum or visceral vascular bed are at least as effectively activated by ingestion, while absorption gathers pace and mesenteric-portal vasculature dilates. In our culture many people feel full, although some feel refreshed or energetic or sleepy: how much does the experience of upper abdominal heaviness depend on the preconception that ingested food swells a bag which lives there,

plus the individual's occasional experience of extreme meals? The receptor mechanism could as likely be hypothalamic or hepatic glucoreceptors, alone or activating a peripheral loop which creates visceral stimuli by altering autonomic tone.

To date, all experiments on the effects of distension or emptiness on food intake have confounded volume of gastric or intestinal contents with speed of intestinal absorption. For example, the observation that a large non-nutritive preload will reduce shortly subsequent food intake is certainly a "volume effect", but at large volumes the clearance of the stomach is an increasing function of the mass in it. The necessary experimental technique has only recently been introduced: Hall (65) has using temporary pyloric ligation to test the effects of preloads on water intake, and finds effects which support a postgastric (postabsorptive?) mechanism over a stretch satiety mechanism.

Nevertheless, the sensations which for a given person (or animal) regularly occur once appetite is released or satiety produced may well augment the motivational state at psychophysical or electrophysiological intensities below innate aversiveness. Neutral sensations probably acquire aversive or appetitive properties by conditioning, and so come to elicit somatic or autonomic (162) respondents which affect intake and nutrient processing (e.g. changed rate of gastric evacuation or insulin secretion). They also acquire discriminative control of operant aspects of food intake. When, in the rat, orosensory control of meal size is first acquired and then reversed, apparently non-oral discriminative control proves to have been established at second reversal of the flavour-nutrient contingency (48). Thus intake can come under the control of visceral stimuli which develop during the meal and vary with nutrient composition.

Normally these internal discriminative or conditioned stimuli compound with pre-ingestive stimuli, or (in more cognitive language) we use social or sensory information

about foods and feeding to interpret or attribute properties to sensations and moods. The discriminative potential of an internal state established by food deprivation is well-known in animals, e.g. (9, 198), although even in the human case we should not assume that different levels of energy need produce readily discriminable sensations, for metabolic adjustments following the absorptive phase tend to keep energy flow to nervous and other lean tissue more nearly constant than during absorption of the last meal.

Individual differences in discriminability of internal states could be important even if the motivational significance of the stimuli is acquired and compounded. There is evidence for substantial variations in sensitivity to motility around a stomach balloon (63), volume of load (41) and intestinal gas or its motilising effect (92). Individual differences in contingencies between food states and body states, such as imposed by some who take care of children (38), will disrupt appropriate association according to standard conditioning principles (138) and risk some of that loss of control only a very modest degree of which is sufficient in the long term to generate obesity or malnutrition.

"Osmotic" anorexia

Colligative effects (dependent on the number of molecules or ionic particles in unit volume of solution) have been the bugbear of animal appetite research since sucrose diets and synthetic liquid diets based on concentrated glucose were introduced. Harper and Spivey's (66) warning was elevated into an "osmotic" theory of satiety by M. H. Smith (165), following McCleary (109). The colligative effect must be in the gut because glucose in normal amounts parenterally has no appreciable osmotic effect and, unlike salt, does not induce thirst in water-replete animals (81). Davis, Collins and Levine (44) have constructed a quantitative control model of intestinal distension as an appetite-suppressant signal resulting from osmosis into the lumen. The model was

established on data from the drinking of sweetened solutions of the nonabsorbable sugar mannitol but proves to have considerable predictive range (45).

The intestinal distension effect is important in pathological "dumping". However, natural macromolecular nutrients do not cause the gut lumen to deviate appreciably from isotonicity during normal digestion. Since soluble polysaccharides (maltodextrins) became available, there has been no excuse for using sucrose- or glucose-based diets in appetite experiments, and particularly for concluding the absence of a metabolic mechanism from results dominated by the transient colligative action of a sugar (15).

It should be noted that another osmotic mechanism is operative in addition when the diet is rich in sodium salts. Thirst is created by the salt, and appetite is inhibited, but these are dissociable effects (142). However, drinking is not based on fluid deficit in the normal diet-adapted situation. It occurs anticipatorily (51), perhaps by a learned discriminative avoidance mechanism similar to that discussed later for meal size control.

Food stimuli

Those few of us who try to analyse learning in normal feeding find learning theorists conspicuously uninterested in the results obtained by such unfashionable response measures, and in turn find their principles and technology insufficient to deal plausibly with the phenomena. The tricks which organisms are forced to acquire in the interests of the learning theory tradition hardly ever centre on feeding itself. When they do at least concern the approach to food, they are obtained by prolonged starvation and rigidly timed delivery of small portions of a single food. The associative factors in normal intake control have by contrast been established by natural contingencies with relatively unrestricted availability of a variety of foodstuffs.

There is no evidence clearly connecting the main conditioned flavour aversion literature to normal feeding. The one

experimental intake procedure that has become popular - Garcia's daily saccharin drink, and variations on it - may yet prove of some use in preventing wolves and eagles from eating lambs (53). Also, use of the procedure did eventually liberalise prematurely fossilised prejudices about the conditions of learning. These had presumably contributed to the lack of interest in Le Magnen's many reports through the '50s that orosensory control was acquired by association with delayed effects of ingestion (e.g. 95, 96). The currently widespread conclusion that there are prewired biological constraints differing between modes of learning may prove unjustified, however. Close attention should be paid to the spatial (61) and temporal (88) characteristics of stimuli and contingencies, but without the half-second CS-US interval dogma (184). It would also be more realistic to shift the focus from taste to texture and odour, and visual appearance in the case of man and other diurnal animals. The saccharin drink has the additional disadvantages of the confounds to which a nondiscriminative paradigm is subject (129), and a greater chance of relating to thirst than to hunger. The fruit-flavoured juices which are sometimes used in discriminative paradigms are as likely discriminated by odour as by taste but they remain calorically very dilute and hence abnormal foodstuffs.

Important distinctions between unlearned and learned preferences were elucidated by work on innate sodium appetite (90) and learned vitamin appetites (147, 148). However, the deficiencies of salts or vitamins used in such work are rare occurrences in omnivores like man and rat. There have been remarkably few studies of preferences for controlled stimuli induced by common deficiencies such as energy or nitrogen.

Energy appetite The ontogeny of sweet preference has been studied a little (80), but work has hardly begun on the ontogeny of the nutrient significance of oral milk cues, the sight of the breast or the bottle, and the appearance and flavour of solid foods. Nonassociative adaptation to food stimuli is sometimes invoked (71) but remains unproven as an

alternative to associative (unconditioned stimulus or reinforcer) effects of the metabolism of ingested carbohydrate or protein or, if there are any, of innately significant visceral or oropharyngeal stimuli. Starch-paired and perhaps protein-paired flavours become preferred and acquire the power to elicit substantial intake of solid diet in the infant rat (135, 159). In the freely fed adult rat, pairing a taste with carbohydrate ingestion (so long as the carbohydrate is not aversively hypertonic) establishes a conditioned preference for that taste (28). Energy-poor or energy-free foodstuffs establish conditioned aversions, at least after a few hours' food deprivation (18, 24, 33, 48). In direct contradiction to the main conclusion originally drawn from intragastric self-feeding experiments, appetitive conditioning of oropharyngeal cues is necessary for the acquisition of the lever-pressing which pumps food into the stomach (73). Maintenance in the absence of taste or temperature cues may be possible when fluids are delivered to the stomach at rates and compositions which are likely to generate sensations sufficient to mediate conditioned respondents to autoshape the lever-chewing "operant" (compare 154). In fact, so-called general hunger/appetite may largely be "trophophilia" (28), i.e. conditioned preferences for energy-yielding nutrients, or conditioned aversions to energy-poor nutrients which perhaps are expressed only during energy deficiency. Respondent factors are much more important in human behaviour than the Skinnerians imply by their curiously rationalistic practice of assuming a response is an operant until proved otherwise. Operant control is unlikely to dominate human feeding behaviour as much as Teitelbaum (177) once implied by excluding any middle involuntary categories between "reflexes" and operants, while having just expatiated on the involuntary motivating effect of "taste".

Protein appetite After only a few hours' deprivation in the rat, conditioned sensory preferences are established by protein or balanced amino acid mixtures (20, 30, 159). Diets relatively lacking in an essential amino acid, or even

perhaps low in balanced protein (21), establish olfactory or gustatory aversions (30, 31, 195). As has been argued for vitamin appetites (147), the protein appetite may be merely the converse of the deficiency aversion. In any case, the effect causes selection of good protein rather than bad protein or no protein. The poor diet may deplete a critical protein (160) in the brain (105), possibly in anterior ventral cortex (32, 106). For chemoreceptors, this would be unusually close to the amygdaloid regions thought to be crucial in learned sensory control of feeding (143). Protein appetite would provide a powerful control system (as yet not quantitatively modelled) to keep the omnivore on a dietary mixture in which amino acids affect feeding only as energy sources. An alternative nonspecific anorexigenic mechanism for the effects of amino acid disproportion (106), perhaps based on ammonia toxicity (123, 158), is less well evidenced and would be less powerfully adaptive. Protein appetite has been tentatively included in a computer model of human feeding, with normally minor effects on the simulations (108).

Basal palatability

Feeding rate, averaged over periods of a minute or more, is a joint function of the competition with appetite from other candidate motivations and the appetite-specific effects of palatability, as affected (via conditioning) by past nutritional status and (via compounding with interpreted internal stimuli) by current nutritional status. At finer temporal resolutions, ingestional behaviour like chewing or licking generally occurs in bursts, with intervening activities like talking or grooming (with forepaw or serviette). It has been claimed that, in both man and rat, food qualities and duration of deprivation affect the intervals between bursts and not the frequency of movements within bursts, but the literature remains contradictory (69). With so few data on foodstuff-specific effects of deprivation, change of foodstuff, and prior experience, we seem a long way from the quantitative description of the intake pattern during a mixed meal, although cumulative intake of single

fluids has been quite accurately modelled (45). Intake rates and nutrient compositions averaged over intervals of a minute or more are probably sufficient for modelling physiological consequences, however. Furthermore, only extremes of palatability or unpalatability have marked effects on initial intake rates (194), possibly because involuntary ingestatory reactions to the less extreme other sensory aspects of the food in question generalise from such thorough prior conditioning. Serious problems arise only if foods varying widely in energy density are available, in which case the interaction between preferences and portion size control would determine how constant energy intake rate remained.

The complexities of the approach phase of appetite have been crudely lumped under an "availability" parameter in our systems models to date: the physical withholding of food from the rat is equated with psychosocial restraints on the timing of meals in man. The search for "conditioned hunger" in the drive theory tradition (79, 117) usually focussed on conditioning the timing of feeding onset. The poor results may derive from an arbitrarily narrow concept of specific drive, unrealistic to the temporal characteristics of internal stimulus change induced by energy need (116). As we shall see next, very strong conditioned hunger effects can be obtained if the rapid stimulus change of energy need reduction is used. Ecological systems analysis of feeding onset is discussed later.

Portion size

Control of the amount eaten is probably far more influential than preferences and aversions in everyday adjustments of intake. Furthermore, nutrient-induced control of portion size is almost the only way in which nutrient physiology can affect human food intake: human preferences are very labile and are obscured by variety in meals; the timing of meals is usually under social control, either directly or via longterm habits; and the amount to be eaten is largely fixed by the time the meal menu or the dessert course has

been selected. Even in the rat, anticipatory control of the amount selected may be the main expression of physiological need: the accuracy of our model with learned meal sizes (below) supports such a conclusion. Garrow (54) concludes that in man the only control of energy balance is deliberate adjustment of intake. The present suggestion is similar, with the qualification that an undeliberative and even unnoticed degree of operant or respondent control may be acquired - with implications for therapy of obesity and anorexia which may be more hopeful than the rather moralistic import of a view that slimming is basically a matter of rational decision.

Without acquired control of meal size, appetite would soon be lethal. When an energy- or protein-rich food became highly preferred (if its sweetness or creaminess did not already make it so), its intake rate would produce a very large meal before an innate satiation mechanism could operate. When a poor food became less preferred, its palatability would habituate out or be reduced to zero by innate satiation before sufficient intake had occurred to meet current need or to prevent acquisition of additional deficiency aversion.

The metering mechanism should operate on the processes ending a meal, not on the basal preference, e.g. initial intake rate. Acquired orosensory control specifically of the rate of intake towards the end of the meal has recently been demonstrated in rat (18, 24) and in man (27). The learning mechanism is powerful in that oral control is rapidly acquired and re-acquired (extinguished or reversed), once any early aversion/preference influences have been overcome. Failures to observe anticipatory orosensory satiety (139, 163) are attributable to the extreme deprivation schedules used.

The acquired behaviour may be a conditioned respondent, i.e. sensory satisfying power. However, "conditioned satiety" is regrettably a misnomer: the response is more likely to be discriminative avoidance of under- or over-satiating after-effects of intake, a learned operant. One possible mechanism is that the discriminative stimulus compounds with internal

stimuli (sensations) which develop before or after innate satiation (metabolic deactivation) is reached: thus the effective behavioural and subjective satiety threshold may after learning be reached sooner with an energy-dense food and delayed with an energy-dilute food. Even such a hazy suggestion is better than obscure invocations of "oral metering", or even some derivation of oral metering from conditioned aversion phenomena (148).

Acquired sensory control of amount ingested sits uneasily among the more familiar types of learned responses. The paradigm can hardly relate to Pavlov's "inhibition of delay". It may have affinities to schedule-induced polydipsia, but that is to explain one mystery by another. The phenomenon is of course the "conditioned hunger" (at least in an intake measure) that most people had given up hope of seeing (117). Note that reduced intake in Garcia's saccharin drink procedure confounds palatability conditioning and satiation conditioning (18). It is only when two-stimulus tests are used that the evidence is provided that lower intake is completely or largely attributable to relative aversion (95, 98). Recent data suggest that decrease of intake conditioned by LiCl may have a small acquired satiation component (45).

To the extent that people do control the amounts they take, to what end do they do it? Is it to avoid the distress of either overeatiation or undersatiation soon after a meal? Is it to provide a convenient period of lack of desire for food, to avoid distractions until the next mealtime, to permit activities other than food-seeking, etc.? In our model of feeding control, we have taken the peak energy flow following a meal to be the reinforcer. Alternatives include total energy yield or delay to the return of appetite, but these may be physiologically more complex, as they appear to require an integrator of energy flow from one meal separate from storage from previous meals, and a clock, respectively.

Until we have characterised the reinforcer(s) or error signals precisely and quantitated their role, it will not be clear whether apparently non-homeostatic influences on feeding (e.g. the emotional meaning of food) are in fact idiosyncratic expressions of the affective side of biological reinforcement. For example, the avoidance of low energy flow may have been made abnormally important for some people: according to our computer model, such a system would slowly but surely get fat if nothing else changed. The reinforcers used in behaviour modification for weight reduction are unlikely to produce stable behaviour unless they are systematically related to the physiological substructure. To take another example, in anorexia nervosa the predictive compound stimulus from food and from the body may be used to maximise the desired consequences, giving a sense of skilled control all too similar to the racing driver's life of dicing with death.

GASTROINTESTINAL TRANSIT

Appetite and body weight may both be ruled by the stomach, but in a way different from that which preoccupied Cannon. The biggest single influence varying the bodily processes affecting appetite and its learning is the relation between the amount in the stomach and the current rate at which the stomach pumps its contents into the duodenum. Given the reserve capacity of digestion and absorption, this normally determines the rate after a short delay at which nutrient is absorbed, which rate in turn is a major determinant of nutrient distribution around the body. Under constant conditions, the gastric clearance function appears to be a remarkably stable individual characteristic (62, 83). It is relatively independent of the macronutrient composition of the dietary energy (78). All the other mechanisms involved may well have constant characteristics, so long as one includes among the constancies functional characteristics such as hormonal responses and their adaptations, learning mechanisms, etc. The feedback structure of the rest of the system will often stabilise system parameters such as average daily intake and body weight or adiposity.

Something similar was suggested by Soulairac (169), although at that time the control of absorption was less well understood and the evidence was inadequate. Also, Snowdon (168) pointed out that gastric emptying time (not a very convenient concept (177)) is a good predictor of intervals between meals in the rat, although his theory of intestinal "dumping" probably has only limited applicability. Furthermore, experiments using vagotomy (5, 135, 168) are generally uninformative as to normal control mechanisms, because of the multifarious abnormalities resulting from nerve section.

Most food leaves the stomach at a rate which is a constant fraction of the amount remaining in the stomach, i.e. exponentially. However, the last phase is much faster and may have a constant rate (84), i.e. linear. This departure from exponentiality will be crucial for the timing of onset of appetite, if as data and modelling suggest appetite normally returns as stomach contents and absorption rate become low. Variable starting time values from extrapolation of the exponential phase back to the full load indicate that there is also an initial phase, generally faster, possibly the dumping of a more or less constant volume of chyme before exponential control takes over. Whether this phase finishes during or after a meal, it may be crucial to the timing of the onset of satiety. Therefore the one clear fact, that stomach clearance is mostly exponential, is unfortunately not likely to help the prediction of food intake. The early and late clearance of the technically difficult-to-handle loads or meals of normal energy density, amount, tonicity and consistency must be investigated in man. A square-root function fits our data on gut clearance sampled at 30-min intervals in the rat (35) and a good deal of human gastric clearance data with dilute fluid loads (74). However, it is probably a simplification which only very roughly covers the two or three phases of gastric clearance.

WHOLE-SYSTEM MODELS

Hirsch (1972), Monteiro (1972), Geertsema (1973), Booth and Toates (1974) and Russek (1976), all apparently working

independently, produced mathematical models of intake control in which both physiology affected behaviour and behaviour affected physiology to produce a complete feedback system. There were similarities in some of their mechanistic postulates, but Hirsch, Monteiro and Russek predicted only 24-hr intakes, not meal patterns like Geertsema's and our models. The Geertsema modelling concentrated on the formal requirements for meal-patterned behaviour and made only broad physiological assumptions, without quantitative specification of model functions or parameters according to physiological data. Russek (151) has at the time of writing been elaborating his model to predict meal patterns, with very similar results to us. However, he models the appetite/satiety receptor processes specifically, unlike us, using his particular hepatic glucoreceptor hypotheses and using functions and parameters chosen for coherence in the absence of direct data. We have used functions and values of variables which were derived as best practicable from experimental data on well-known physiological processes within the system or on correlations between physiology and behaviour. Because of these differences and the limits of space, I have expounded only our own model here.

Deficiencies in the available physiological data enforced some very crude approximations on our feeding models Mark 1 (34, 180) and Mark 2 (35). This is an expected occurrence with any model which is the first at its level, because only a working model or an equally specific theory can tell us the physiological measurements and physiological-behavioural correlations which are really worth obtaining. More serious was an embarrassing implication of these early models and a substantial mistake in their physiology.

The embarrassment was that the model appeared to predict feeding directly from current events in energy physiology. This was a considerable encouragement to our approach to the metabolic factors in appetite - a single-factor theory of energostasis or an energy supply signal, to replace the

plethora of glucostats, lipostats and thermostats (15, 16). Yet, on the other hand, our evidence was that learning makes a major contribution to appetite. How could the two approaches be reconciled?

The mistake was that energy was modelled as reaching fat and the appetite/satiety receptor system as soon as it entered the rat's mouth. In fact, there must be a gastrointestinal processing delay, even if the effective lag is only a few minutes. Some food passes from the oesophagus to the duodenum without being delayed and mixed with other stomach contents. Glucose or starch carbon passes from the mouth to the blood, liver and brain of the rat in less than 5 min (134, 172). Adding a gut lag of only 2 or 3 min to Marks 1 or 2 produces inordinately large meals.

Mark 3 of the model is augmented to include both the most important type of appetite learning (i.e. sensory control of satiety threshold) and the necessary delay between ingestion and tissue uptake of energy. Only time will tell whether it is luck, misleading coincidence, or a valid indication just what are the important factors in feeding control - but the resulting simulations are even more accurately realistic and more versatile than Marks 1 and 2.

Feeding model, Mark 3

The structure of the model is outlined in Fig. 1. The computational procedures given below (energy in small calorie units and time in minutes, with apologies to SI) use the method of successive addition, not differential equations. Values of variables should be updated at least every 15 sec of rat time.

1. Gastric emptying Multiply the square root of the energy in the gut by the current clearance rate factor to give rate of movement of nutrient energy to the duodenum. Our gut clearance data for the intact male rat on diets of the energy density of lab chow have suggested factors of around 0.9 in the dark and 0.6 in the light. A linear

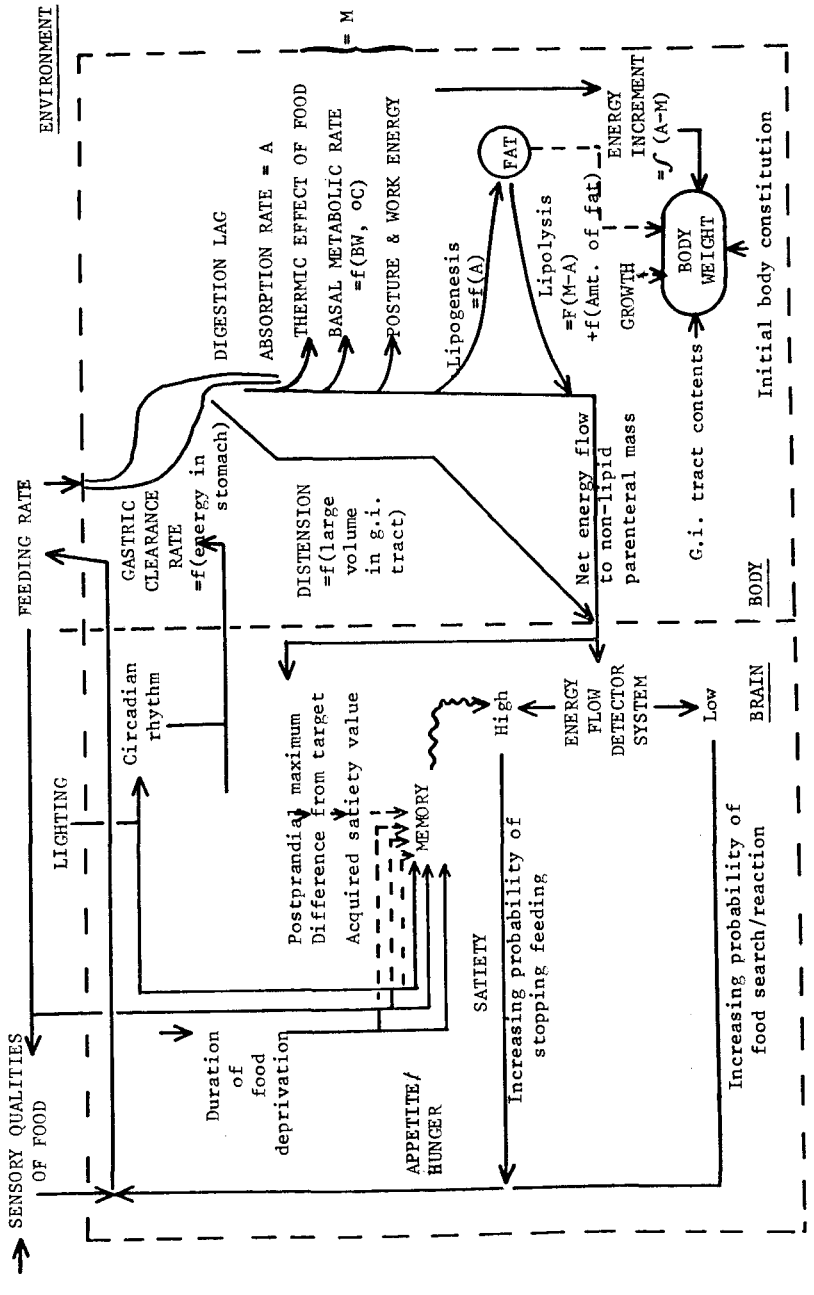

FIG. 1 - Physiological/learning model of feeding and body weight in the rat (Mark 3).

gradation from one value to the other is imposed over 1 hr on either side of illumination change.

2. Digestion Allow a lag of 5 min between ingestion or gastric clearance and the arrival of energy at the tissues. This parameter lumps passage of nutrient through the body, including digestion, absorption and blood and lymphatic circulation, into a simple delay operative after the gastroduodenally determined gut clearance function. When the physiologists have more data on the relevant dynamics, detailed calculations should be substituted for the lumped factor and the square root function.

3. Energy output From the absorptive flow subtract body energy losses, i.e. metabolic rate. The components of MR are:

a. Thermic effect of food, estimated as one-tenth of absorption.

b. "Basal" MR, i.e. postabsorptively and at rest. The 2-hr average MR data reported by Le Magnen et al. (101) for the freely fed rat are roughly simulated when a basal value of 27 cal/min is used (Table 2). When the effects of cooling or heating on intake are simulated, a value can be calculated from the body weight of the rat and environmental temperature (195).

c. "Postural" MR (176, 193), i.e. the energy cost of movement without running or external work (which could be calculated in addition if its simulation was required). A value of 5 cal/min is used throughout the night and around the start of meals by day.

4. Fat deposition and mobilisation Also subtract lipogenesis or add lipolysis ("lipoflow"). In Marks 1 and 2, values derived from respiratory data were used (100, 101). One of the serious limitations was that only 2-hr average data were available, apart from a limited set of 20-min averages having some puzzling numerical characteristics (100). Lipoflow certainly varies greatly around mealtimes. Such transients should affect the simulation considerably. Also, their absence from the model has helped to create some misunderstandings (121). In Mark 2, we occasionally guessed

some lipoflow transients, e.g. to model the large first meal after unexpected deprivation (35). We hope eventually to have fatty acid and carbon oxidation flux estimates over radioisotope incorporation periods of a few minutes, but Mark 3 has had to lift itself by its whiskers and use estimates of lipoflow from absorption which produce realistic 2-hr lipogenesis-lipolysis averages as well as realistic meal patterns. We used the simplest linear equations which reflect what is know qualitatively about the effects of absorption and fat cell size.

a. Above an absorption rate of 50 cal/min, three-quarters of the energy flow above that rate is diverted into lipid synthesis and net deposition.

b. On the other hand, when absorption falls below MR, net lipolysis adds energy to the flow from absorption. The lipolytic pressure is represented as one-quarter of the deficit in absorption rate below MR, i.e. lipolysis of about 7-8 cal/min at zero absorption.

c. Cumulative net lipoflow gives adipose gain (at 8 kcal/g).

d. The size of the adipose fat store probably affects lipolysis, although the mechanisms are not clear (114, 136). This feedback from fat is represented as extra lipolysis of 0.1 cal/min for every gram of adipose triglyceride. No set-point is assumed. In simulations of intact freely fed rats, the effect on food intake is very small compared with that generated by short-term control. In rats simulated as obese, e.g. after force-feeding, the inhibitory effect on intake is of course substantial, and produces a return to around normal adiposity which is then stable. This model thus poses the problem of identifying longterm regulatory mechanisms as the need to measure shortterm feedback metabolite flows from fat, on the average small and perhaps only approximately related to cumulative changes in energy storage.

5. Large stomach volume Add an inhibitory influence of gut distension, as follows:

a. Calculate volume of gut contents by counting every gram of food as 1.9 ml of chyme (127).

b. Add an energy flow of 1.5 cal/ml for every millilitre of gut volume above 5 ml. This is a function which was extrapolated from electrophysiological data on gastric mechanoreceptors (35).

Doubts as to a role for distension in normal food intake were expressed earlier in this paper. The simulated effect of distension is almost negligible in freely feeding normal rats (average meal size is about 0.2 g smaller). However, it realistically stops the computer bursting its stomach when food energy is very poorly satiating because of diabetes (180) or other troubles.

6. Energy flow thresholds Compare the net energy flow to receptor-containing nonlipid parenteral mass (NLPM) with threshold values at which eating is likely to stop or (if food is available) start. Eventually it should be possible to simulate the energy flow (or the proximal stimulus it determines) to the presumably small subcompartment of NLPM which serves as hunger/satiety receptor tissue. Meanwhile, absorption or infusion correlates of feeding onset and offset indicate that a flow of around 20 cal/min (1.4 watt) into the whole NLPM stops intake and a flow of around the same value out of the whole NLPM releases intake. The receptor itself need not be a store capable of releasing energy into the circulation in the way that the liver releases glucose and muscle releases amino acids. It might for example operate with a single threshold of an energy uptake which is maintained in the absorptive phase but cannot be maintained under postabsorptive conditions. Values of -20 and +20 cal/min were used as classical thresholds and simple step functions in Marks 1 and 2. In Mark 3, the signal detection problems the real system must have are represented as random walks of the effective thresholds around these values of central tendency. A step of 1 cal/min is made on each calculation cycle, either up or down, with equal probability at the central value, and certainly towards the central value at the limit set for

the walk, probability varying linearly between centre and limit.

a. Randomise the onset value for each meal.

(i) The organism's problem of identifying its internal state of energy need is represented as limits on the random variation of onset values at ±10 cal/min. An additional range of ±5represents two influences which should be explicitly modelled when enough is known: (ii) Sleep and other incompatible activities may delay feeding (allow net energy flow to go very low); (iii) Extraneous stimuli may activate feeding in advance of spontaneous onset (allow feeding before energy flow has reached the spontaneous threshold).

b. Calculate the offset value to yield a maximum net energy flow of 20 cal/min after the meal. Until we know more about what is learned, acquired control of meal size is represented by a fool's superposition theorem. The offset value used in the last meal under the same conditions (of lighting, deprivation and food flavour) is adjusted down by the amount of overshoot after the last meal, or up by the amount of undershoot below 20. This acquired offset value is also randomised within the limits ±5 to represent the memory recall problem and within additional ±10 limits to represent the internal state detection problems.

7. Feeding rates If food is available, select a foodstuff of specified energy density and eat it at a rate determined by its sensory characteristics. Chow intake is simulated at a constant rate of 0.3 g/min in intact rats. Conditioned preferences and competing motivation can be represented at this step in calculation.

Hopefully, the associative theorems of Rescorla and Wagner (138) will be applicable to acquired sensory control of both preferences (calculation 7) and satiety threshold (calculation 6b). Uttley (183) has shown that they are equivalent to a hypothetical learning "unit" for which there is direct neurophysiological evidence (10) and which shows considerable versatility when combinations of units are programmed in a

computer simulation. That is, a quantitative physiological reductions of the learning loops to the neural network level are conceivable.

The double classical threshold system in the model has some mathematical isomorphism with a set-point mechanism. However, no such comparator mechanism is required to produce the modelled tendency towards zero energy flow. The formulation that there is a two-way detection problem for the organism is intended to imply less complex processes, such as a mechanism which changes the state of the appetite/satiety system when a receptor is activated when its metabolism (say) departs from an equilibrium range in either direction.

8. Body composition Cumulative difference between intake and metabolic rate gives total energy gain. Cumulative lipoflow and cumulative flow to NLPM give adipose gain and lean growth respectively. A rough estimate of body weight gain is provided by adding gut contents (1 g/ml) and energy gain (1 g/6 kcal) to the body weight of the rat ready-to-eat at the start of the simulation.

TABLE 2 - A sample prediction by Mark 3 model of feeding and metabolism over 10 days in intact freely fed rat.

	Dark phase		Light phase	
	Model rat	Real rats	Model rat	Real rats
Average meal size (g)	3.1	3.1, 2.9	2.5	1.6,2.3(81)
SD (% of mean)	26	71	16	75 (81)
Average meal-to-meal delay (min)	190	160	258	218 (81)
12 hr Average MR (cal/min)	35.8	38.6	30.4	31.2(82)
Most extreme 2-hr lipoflow	-9.4	-9.7	7.0	8.3(82)

WHICH ENERGY FLOW? - AND HOW IS IT DETECTED?

There are many unanswered questions about the biochemical character of the energy-yielding metabolites which inhibit appetite. Until quite recently, the only nutrient which

received serious attention was glucose. It has therefore been important to show even semi-quantitatively that other sources of energy suppress food intake by appropriate amounts. A number of nutrients other than starch or glucose inhibit feeding when ingested, intubated or infused in normal amounts or at normal rates (16, 26). However, some are readily converted to glucose e.g. fructose, glycerol, alanine. Yet, although substantial gluconeogenesis is likely to have occurred between loading and satiety test in such experiments, conversion to glucose is unlikely to have been as complete as implied on this interpretation by the caloric compensation observed (16). Some nutrients or energy-yielding metabolites suppressing feeding are not themselves converted to glucose but do help to maintain hepatic glucose output, as indeed do the potentially glucogenic substrates without conversion of their carbon to glucose. Examples are ethanol and short-chain fatty acids (16). In any case, whether or not by glucogenic and glucose-sparing mechanisms, a wide range of small MW energy-yielding substrates are satiators. We need many careful experiments to determine whether energy-yielding metabolites are freely exchangeable as satiators, and whether it is glucose maintenance, ATP yield, or some other function which best predicts satiating effect.

Fats

A most difficult question at present is whether or under what conditions long-chain fatty acids and triglycerides act to suppress appetite. A Randle-type effect of fatty acids on glucose metabolism controlling feeding (100) might generate a supracaloric control signal. This now seems to be excluded by experiments on fatty acid infusion in rats (23). On the other hand, medium-chain triglycerides strongly suppress food intake (D. A. Booth, unpublished); these are highly ketogenic, however. Furthermore, gastric loads of soap or oil may be anorexigenic because of gut distress rather than by activating normal postabsorptive satiety mechanisms. Le Magnen et al (101) treat lipid and

non-lipid energy as equivalent in their effect on feeding, as also do we in the series of computer models to date. Parenteral fat suppresses appetite in man (95). Yet Booth (16) assumed subcaloric effects of long-chain fatty acid load because of partly non-oxidative or even incomplete metabolism, and the single datum was consonant with the assumption. Furthermore, Nicolaïdis and Rowland (in preparation) found that where Intralipid or Lipophysan triglyceride was tolerated intravenously neither intake decreased nor weight increased, suggesting poor metabolism. As with all infusion experiments, the physiological status of the animal is of course critical to the pattern of infusate utilisation and hence the effect on feeding. Rowland, Meile and Nicolaïdis (146) themselves have shown that Adair, Miller and Booth's (1) lack of definite effect of continuous intravenous glucose infusion can arise from a distribution of effect between feeding depression and body weight increase, which is shifted to accurate caloric compensation in feeding by the co-infusion of insulin. Indeed, contrary to impressions generated by the feeding elicited with large doses of insulin and by the failure to show that insulin was involved in the intake-suppressant effects of nutrient loads because they had colligative gut effects, insulin is normally a hormone of metabolic satiety. The rat's insulin secretory response has acutely little reserve and may under some conditions need supplementation to show post-absorptive satiation (25). Timing of infusion in normal relation to meals may also be critical. Similarly, with triglyceride infusions, we may need to control the infusion schedule and cofactors such as lipases and their activation by pre- or co-infused heparin and also the apoproteins and other fats associated with physiological circulating triglyceride. Good infusion experiments could modify the single-factor energy supply theory considerably, despite the success of the current version at conflating short-term and long-term stabilising mechanisms. Results may be obtained in man (85).

A unitary signal?

The experimental designs which could give precise data on the effects on appetite of current energy supply to tissues are now just about practicable, and hopefully will be run in the next few years. At the moment we have qualitative data - and a general model. The model behaves realistically on the basis that appetite is released when a net flow of energy from non-lipid parenteral mass begins to be detected and is suppressed when net flow into NLPM is detected. That does not imply that the appetite/satiety receptor system itself (the body-nervous system interface(s)) detects all energy-yielding metabolites, or even any metabolite at all. The implication is only that some tight correlate of NLPM energy flow affects the receptor(s). A hormone could do the trick. There is now a single piece of direct evidence, from anti-insulin serum injections, that insulin levels in medial hypothalamus affect feeding, but other evidence is hard to reconcile with a simple insulin signal (174). Hormones released from the gut during filling or absorption must be considered, particularly cholecystokinin (163, 164). A neural signal from the stomach or duodenum reflecting the current rate of energy absorption is another neat possibility (75). However, no gut influence is essential to postabsorptive satiation (26). Furthermore, our model is realistic only when it includes energy flows in addition to the flow from the gut. If a single metabolic signal is sufficient to explain the facts, the use of Occam's scalpel in the dissection of appetite mechanisms might save unnecessary chasing of multiple appetite/satiety signals.

If Russek's (149) perihepatic glucoreceptors are the only ones important to appetite (an hypothesis he has slightly qualified (150)), then indeed the appetite/satiety receptor is effectively in a NLPM energy store, directly measuring liver glucose uptake and release, which hopefully correlates well with muscle amino acid uptake and release. If on the other hand the receptor(s) are in the brain, however

atypical the region we would not expect the receptor tissue to export energy, although it could well consume local substance (57) as appetite becomes due. It is therefore important to determine brain regional energy flows in putative receptor regions. The hypothalamus might have unusual types of glycogen or protein reserve, or there might be lipid stores (surprisingly for brain) or functional variation in membrane lipid composition (122, 132), whether or not they "model" peripheral adiposity as Panksepp (132) has suggested. Butterfield's (39) study of AV glucose differences was early evidence that the human brain contains insulin-sensitive regions. There is now abundant evidence for insulin-sensitivity in brain tissue associated with meninges (136) or in periventricular regions known for blood-brain uptake peculiarities (128, 161). We have begun to estimate regional glucose metabolic fluxes, and find a distinctively rapid rise in hypothalamic glucose consumption *in vivo* following a meal (J. C. Newman and D. A. Booth, unpublished data). It remains to be seen if Mayer's classic concept of an insulin-dependent glucose-sensitive satiety/appetite receptor in the brain (if not VMH) survives: insulin-dependence or sensitivity has been dissociated from glucose-sensitivity in the rat brain for feeding (161), unit firing (128), and the hypoglycaemia induced by cephalic insulin (175). Also, non-glucose substrates must not be considered: ketone bodies can be used without adaptation to starvation (52), although 2-hydroxybutyrate does not appear to be a strong satiator in adult rats on ordinary chow (D. A. Booth, unpublished data). It must be emphasised that the energy-flow model does not at present include specification of receptor processes at the cellular or even at the tissue level. It serves only to point up the possibility that there is a unitary receptor system which functions as a monitor of total NLPM flow. Non-receptor tissues are likely to serve within the whole functional system to transduce energy flows of various sorts into the signal(s) acting on receptor tissue itself. In particular the liver would be expected to play such a transducer role.

Also, the focus on NLPM flow implies that control of the partition of energy-yielding metabolites between lean and adipose mass will have powerful effects on appetite as well as on body composition. Classically, insulin and growth hormone have been considered major determinants of this partition; some relevant data have recently been reviewed (191). When we can model the control of the secretion of these and other influential hormones such as glucagon (the energy metabolites themselves dominating phasic control), our model's crude linear lipoflow dependencies on absorption can be replaced. More accurate and versatile modelling of longterm intake and body weight effects should result.

Energy from amino acids

In our own models to date, amino acids have entered solely as their energy equivalent on oxidation to urea. In the slowly growing mature rat (and man) on a diet adequate in protein of good biological value, this is likely to be close to the truth - that is, a good approximation to short-term effects. However, Webster (186) has suggested from data in Zucker rats and in farm animals that intake is limited in the long run only by the rate at which the organism can carry out the work involved in synthesis of body constituents. About a third of this work is protein synthesis. As the organism tends to stabilise adiposity (the ratio of adipose to lean tissue), feeding on an adequately balanced diet sustains optimal growth of lean body mass.

Rat and man are omnivores, however, and are in principle liable to take a mixed diet which is unnecessarily high in protein or is poor in protein, or even badly proportioned in its amino acid composition. Nitrogen output changes rapidly in an adaptive direction when nitrogen input is inappropriate (in contrast to the case with energy input and output). Liver enzymes change in concentration or activity and urinary nitrogen follows to a plateau within a day or so in the rat (e.g. (43)). Nevertheless, there is considerable potential also for compensation in nitrogen intake. When poor palatability or energy requirements do not override,

rats can adjust their intake of protein-poor or protein-rich diet (21). This may be achieved by the very powerful feed-forward control mechanism of acquired protein appetite, discussed above, of which quantitative model remains to be built.

FOOD INTAKE RHYTHMS

Circadian variation

Most feeding occurs in the part of the 24 hours when the organism sleeps least. This is true of many species, including the nocturnal rat and the diurnal human being. The idea that sleep is to conserve metabolic energy has recently been revived (197). In the short-term, there is an extraordinarily high correlation of feeding with the previous night's REM sleep in the rat (157). A correlation of somnolence with satiety is widely believed. Is sleepiness an autonomous motivation competing or time-sharing with appetite or do they specifically trigger one another? The dichotomy is probably false: very weak interactions between initially autonomous oscillators can be sufficient to bring them completely into phase (126).

Our model shows that visceral activation during the behaviourally active night phase is sufficient to explain the circadian variation of the food intake pattern, MR and lipoflow in the rat. By "visceral activation" I mean at least the acceleration of the gastric clearance rate for given contents of the g. i. tract, with the consequent facilitation of exocrine secretions. The insulin secretory response to a given blood composition might be augmented too, but it is not necessary to postulate such an effect within the model of the normal rat because in that simulation sufficiently great nighttime lipogenesis arises from greater nighttime absorption rates.

There are two mechanisms represented in Mark 3 which account for the fact that food is less satiating in the rat's night (100, 102, 130). (i) The fast gut clearance function produces more lipogenesis for a given size of meal. (ii) Greater motor activity by night causes more heat loss.

Both lipogenesis and heat production divert energy from the appetite/satiety receptor system, so attenuating satiation. At least the energy expenditure difference between active and inactive periods exists in us. In a prototype model of the control of human feeding by internal energy flows (108), the difference accounts for 3 meals a day and yet no hunger by night.

Rats on a 2-hr lighting cycle eat more in the dark than in the light, although the proportion is attenuated (36). A weakened circadian rhythm of feeding and activity also persists. Our model predicts the same pattern, because any lighting cycle which permits entrainment of gut clearance should produce more intake in the dark, and yet this rhythm should be lower in amplitude than that on circadian lighting and a weak circadian feeding rhythm should persist, because the endogenous circadian activity rhythm diverts more energy from satiation in the active period.

Oestrous cycle variation

By a close analysis of feeding patterns in mice, Petersen (133) has identified two major factors in the variation in food intake around the oestrous cycle and the body weight difference between the sexes. The data are consistent with less detailed findings in the rat (7). Intake is reduced during sexual receptivity by an increased distractibility. This presumably might be represented as effects of motivational time-sharing on feeding rate and the timing of meals: in our model, increased randomness in meal onset time will tend to produce the observed lower meal size by raising the average starting gut contents. Secondly, Petersen identified an estrogenic failure to compensate intake in metoestrus, which he attributes to a changed body weight "set point", as do other workers. The meal pattern and the body weight effect can be accommodated in our model as a slowed gut clearance function. If this is mediated by the VMH, like the effect of lighting on oestrus (185), that would also explain the similarity of hyperphagia in males and females after VMH lesions (58), attributable to loss of daytime slowing of the stomach.

Menstrual cycle variations in stomach clearance rate and taste reactivity (192) have been evidenced in man (if some readers will pardon the expression). It is not clear whether there are human food intake effects to be explained.

BRAIN PROCESSES CONTROLLING FEEDING

A brain researcher who has got this far may be bored or offended by so much "peripheralism" in appetite. Neither attitude would be justified. Brain mechanisms would be exploit in our model if there was a single piece of useable information on the neurophysiological processes controlling appetite from 30 years of the "centralist" approach to feeding.

In fact, the old centralist-peripheralist controversy is a completely unproductive pseudo-question. The desire for food is a motivational organisation in behaviour - that is, present and past relationships between the organism and its environment. As such, the physical basis of appetite/hunger cannot simply be a "central motive state" in the brain or a "sensation" in the body. Especially in the case of behaviour critical to body integrity, we must not be surprised to find controlling variables outside as well as inside the brain, in body processes and in environmental chemistry.

There are quite clearly several processes in our model, and in most theories of feeding control, which are in principle reduceable to neural processes, but we lack the data on brain activity in relation to behaviour and to the rest of the body which are needed to choose amongst an arbitrary number of theoretical options.

Indeed, our ignorance about even the behavioural and peripheral structure of feeding control, despite their greater accessibility, has been sufficient for simple experiments to be extremely productive. Further sophistication of these behavioural and peripheral physiology explanations is probably a prerequisite for experiments which could yield interpretable brain measurements. That is why my own

approach to feeding control included virtually no brain measurements for 8 years. Maybe the reader of this book can discriminate whether the field is on the brink of a maturity in which environmental, peripheral and central approaches can begin to be integrated or whether it still has to grow for years or decades more through an adolescence of homeostatic speculations, contradictions, fascinating artefacts and qualitative demonstrations.

What types of experimental data are needed if we are to construct a working theory of the brain processing of information in the control of food intake?

Lesion phrenology still dominates the journals. There are of course motives for lesion studies other than finding out how the brain does its job. Brain-damaged preparations are kaleidoscopic intellectual puzzles - another shake, another paper. They can also provide tests of certain sorts of purely behavioural theoretical statement (125, 178). Surgery can crudely simplify a physical system and may create novel phenomena, but this still identifies no process. Doing it blind to the system's normal workings can create uninformative analogies and malfunctions, and may be a justifiable approach only when we remain incapable of successful manipulation and measurement of controlling processes in the normal range of operation of the intact system (no longer the case in appetite science). The brute fact remains that a behavioural change following brain damage cannot in principle tell us anything by itself about the brain processes controlling such behaviour. A lesion experiment can only carry neural process implications when it has been carefully designed to provide a critical test of some aspect of a theory which successfully coordinates neuroanatomical structure, neurophysiological transfer characteristics, and behavioural input-output relationships (187). Otherwise the most that "localisation of function" by damage (or by physiologically unmonitored stimulation) can provide is a risky basis for selecting the first part of the brain in which to start asking questions about neural processes controlling that "function".

After 35 years of animals with ventromedial hypothalamic lesions and 25 years of lateral hypothalamic animals, not an hypothesis of hypothalamic processing survives based on such preparations. One important notion - arousal-dependent sensory reactivity - tells us (as one would expect) of the existence of processing outside the hypothalamus. Even then, the integrated arousal need not influence reactivity through the hypothalamus; another route subject to inhibitory or facilitatory influence from hypothalamus is equally feasible.

A great deal of behavioural study has been invested in the brain-damaged preparations, and - more recently at least in the VMH preparation - some limited biochemical measurements. Paradoxically, the results do provide a range of data into which a theoretical system whose peripheral physiology is exploit can dig its teeth (see below). The conclusions are still nothing as to brain processing.

It must be said that "chemophrenology" suffers as serious a deficiency. Findings that some drugs specifically affect feeding or some aspect of it identify by themselves no particular brain process. Blundell's (11) contrast between the effects of amphetamine and fenfluramine on the rat's meal pattern put important constraints on the behavioural account of the pattern, but do not tell us what noradrenaline and serotonin might be doing neurophysiologically to affect feeding. Lesion chemophrenology (cf. 6HDA) or stimulation chemophrenology (115) provide a place as well as a chemical but still no process by which local output can be calculated from local input.

I must hasten to add that "electrophrenology" also exists. Unit recordings can be made which tell us nothing of the information processing mechanisms underlying behaviour - for example, the mere detection of a change in firing rate in a specific region of the brain in correlation with distinctive movement output, sensory input or specific acts. Even evidence of the routing of such influences, by methods varying from lesions to collision demonstration, simply poses

questions as to mechanism. Rolls (145) for example formulates a sophisticated electrophrenology of feeding, on which it may be possible to design experiments which begin to provide the transnuclear or interneuronal transfer functions which are necessary before we can even begin to formulate a theory of the neural processing which controls appetite. Mogenson's (118) and Norgren's (124) combinations of neurophysiology and neuroanatomy promise to move in the same direction.

THE LATERAL HYPOTHALAMIC PREPARATION

It has long seemed likely that the lateral hypothalamic syndrome reflects the disruption of more than one neural pathway or relay. The anatomy of the lateral hypothalamus (64, 120) puts the onus of proof on those who claim otherwise (50). Arousal-dependent sensory neglect (190) and a permanent disruption of fluid control (50) must both be important in the appetite of the LH rat. Slowed stomach emptying could be another major factor in the syndrome. The highly stressed, immobile LH rat looks a good bet. Maybe the lesion produces a functional vagotomy, resulting in splanchnic overinhibition of the clearance function. Recovery of feeding after vagotomy in rabbits has similarities to recovery from LH lesions in rats (141). Gastric clearance function should be measured in acute and recovered laterals (the rats should be force-watered to remove dehydration artefacts from the gastroduodenal processing). Rowland (144) has noticed full stomachs when he implants gastric cannulae after LH rats have eaten no more than 1 g for many hours.

A sufficiently slow stomach might by itself produce long meals at short intervals (largely under distension control). Slowed eating, because of reduced sensory preferences and dry-mouth difficulties in mastication, would easily combine with a more modestly slowed gut clearance function to produce the LH night nibbler and day starver. The relative stability of body weight at levels below control after small LH lesions (86) could in our model follow from the long-term self-steadying consequences of a shift to a slower stomach.

THE VENTROMEDIAL HYPOTHALAMIC PREPARATION

The obese hyperphagic rat with lesions in or near the ventromedial hypothalamic nuclei lacks the normal daytime suppression of intake. There has been a gathering convergence of evidence that hypersecretion of insulin is critical to the VMH syndrome: removal of a normally inhibitory influence through the vagus nerve is widely suspected, although to date unproven because of the artefacts arising from gastric stasis following vagotomy. The hyperphagia which occurs while the VMH preparation is getting fat has been attributed to the sequestering of absorbed energy into triglyceride (34, 101). As our modelling became more realistic, however, it became evident that excessive daytime lipogenesis leaves much of the pattern of overeating unexplained. The addition of a daytime gut clearance function as fast as the normal night function in a Mark 2 simulation of the VMH rat filled the gap. We therefore predicted that another major abnormality to be found in this preparation was rapid gastric emptying by day (35).

Teitelbaum (177) has suggested that the VMH preparation may be insensitive to gastric distension, as it takes larger meals and as effects of distension have been recorded in the VMH. However, as he pointed out, more must be involved, otherwise meal frequency would compensate. The gastric efferent abnormality we have diagnosed may be sufficient, even though the preparation retains normal metabolic receptors (35) and conditioned satiety (167), and with these mechanisms the intact system (as modelled) compensates well. Lack of a normal daytime slowing of gastric clearance should produce acute hyperinsulinism secondary to hyperabsorption (even within minutes of surgery with food in the stomach), and chronic hyperinsulinism following adaptation of the beta cell to unremitting rushes of nutrients. Only the most carefully controlled physiological experiment could establish a direct vagoinsulin effect against this indirect mechanism.

With the possible exception of finickiness (which can be anatomically dissociated from obesity (60)), the "paradoxical" feeding abnormalities of the VMH rat are attributable to lipogenic pressure and obesity. The food-deprived static or dynamic preparation has more fat to mobilise and the extra lipolysis will keep motivation low. An extra diversion of energy into fat by augmented secretion of insulin towards the end of a meal (whether secondary to increased absorption or not) will explain the small increase in meal size consistently observed. Invocation of a fat setpoint, let alone dual lipostats, is as unnecessary here as elsewhere.

Static obesity "cures" the hyperphagia and some of the abnormalities in feeding pattern by the extra fat producing an abnormal bias to lipolysis. This keeps the stomach emptier on average and so reduces the duration of very fast flow of nutrient to the body, even if the pathogenically fast day clearance function has persisted. Note that no body weight or fat set-point is invoked - some non-criterial negative feedback is all that is needed. There is no need for the adipose fat-sensitive hypothalamic receptors postulated by earlier control theorists (67, 87) nor a local model of body fat (132). The elaboration of longterm stability from shortterm variations in current energy supply implies that a satisfactorily controlled "pair feeding" study has yet to be run on VMH rats (59) or any preparation, and may be impossible except by an intermittent duodenal infusion technique.

LONGTERM STABILITY OF INTAKE AND BODY COMPOSITION

Physiological regulation of energy balance probably does not exist. Garrow (54) reaches this conclusion from individual balance data over weeks in man, and an equally critical treatment of the data on individual rats would probably parallel it for the smaller and shorter-lived creature's equivalent time period. Even our present extremely crude model illustrates how short-term feedback controls on intake can provide longterm stability of intake and energy storage, if they include even weak coupling to adipose cell metabolism,

without separate and curiously precise mechanisms for measuring fat store size or body weight. In other words, if regulation is worth seeking anywhere, it is in the longterm average of some type of current energy supply to certain tissues, not in energy balance.

Force-feeding, electrically stimulated feeding or insulin injections have been used to test the stability of body composition (and hence of body weight, given a lean structure to maintain) when spontaneity of feeding is restored. (Incidentally, the latter two techniques may work, respectively, by accelerating gut clearance and providing continuous lipogenic "pressure".) The fattened rat shows initially almost complete suppression of feeding and rapid loss of weight, followed by a pattern of small, infrequent meals until adiposity is within a few percent of undriven values (175). These intake and weight effects are produced by the Mark 3 model, because of an increase in lipolysis as a function of adiposity, crudely represented as a linear feedback.

Within our model the feedback from energy stores does not guarantee constancy of body composition of the intact system. It merely tends to produce it against a variety of displacements. Very high or low dietary energy densities, protein contents, or palatabilities, extremes of stress, work or temperature will create a new set of self-stabilising values.

Appetite scientists should impose on themselves the discipline of a 5-year ban on the term "regulation" used in the precise sense advocated by Brobeck (37) which invokes a concept of "set point" from engineering control theory. Not one set-point comparator system has to my knowledge been unambiguously identified anywhere in physiology or human information processing. We should keep to concepts which suit biological and cognitive systems. We know that chemical equilibria and the circulation of the blood exist. Biochemical feedback concepts are adequate to the phenomena, it appears from our appetite model.

Homeostasis similarly should be used as a purely descriptive term for the tendency of a system parameter to return to control value after disturbance. Such stability needs no mechanism storing and communicating a reference value to be defended. The ban should include the muddled distinction between "regulatory" and "nonregulatory" feeding: feedback influences and imposed influences are at work on every mouthful; even a statistical assignment of variance to two categories will founder on the interactions within the controlling system.

ECOLOGICAL MODELS

Feeding behaviour and foraging strategies are intimately related to an animal's ecological "niche". It is now beginning to be possible to calculate an animal's optimum strategy, not just in terms of time and energy budgets (89), but in relation to evolutionary fitness over a species' life history (104) or to a particular environment (156). The costs and benefits of different sorts of food-related behaviour in a given natural environment can be assessed in a unified mathematical function and used to decide optimally between behavioural alternatives.

These ecological models make similar predictions to causative models (156). It has sometimes appeared to have been implied that ecological explanations are incompatible with physiological explanations (42). However, without here going into philosophical questions about reduction, it could be considered a simple fact of scientific life that a system can sometimes be characterised, even exhaustively, at more than one level. The ecologist may be right to describe a genetically determined response of the feeding pattern to natural environmental constraints, and others be right in detailing the link between the genes and the behaviour in biochemical and physiological terms. If fixed-ratio schedules (lab analogues of ecological constraint) are represented as limitations on the availability of food, appropriate changes in the four parameters into which Collier et al (42) exhaustively analyse feeding (frequency

and duration of meals, choice and intensity of feeding) would be predicted by a physiological/learning model. One can agree to deplore overemphasis on the aberrant cases of traumatically assaulted animals and emergency situations, while still presupposing that short-term feeding behaviour is a function of the momentary state of an organism's body and the food, plus its learning history. Hopefully, ecological and physiological/learning models will soon be compared against the same wide range of data and perhaps even interconnected to form a more inclusive theory.

Ruminants

Computer models which include feeding have been developed for farm husbandry (4, 49, 119). These include purely empirical ecological factors. Feeding by a flock of ewes and lambs, for example, is represented (49) as a daily inflow subject to simple algorithms of feedstock availability and preference, to ecological variations such as weather and herbage species, and to management variables such as cost of feed concentrates and time of culling. Psychological and physiological theory have yet to prove that they have more predictive accuracy and range than empirical functions in this context. Perhaps to date there has been little interest or skill in trying them out.

Man

Many cognitive and cultural constraints on feeding can be incorporated in a physiological/learning model as mere data conditions. This is sufficient to illustrate ways in which social conventions and individual feeding habits compromise with underlying biological control. Cuisine and economics strongly determine individual choice, but the familiar foodstuffs would likely not be the accepted ones without the nutrient sensory conditioning mechanisms. Socially determined habit and the clock will constrain the timing of any particular meal, but conventional meal times are probably adapted ultimately to the demands of the average human body and its activities (108).

CLINICAL APPLICATIONS

Aetiology

The tolerant reader must by now be expecting me to float the idea that a major factor in the aetiology of obesity and perhaps diabetes is a fast stomach. It could indeed explain many behavioural, endocrine and metabolic findings in obesity. An abnormally steep emptying function at the earliest or the latest phase of gastric emptying could produce overeating, hyperinsulinism, a tendency to adipose gain, and an oversensitivity to salient external stimuli if desatiation raises the level of general arousal. Hunt has pointed out that at the higher end of the dietary energy density range, the earlier stages of gastric emptying do not slow down in proportion to energy cleared, and indeed leaner people do tend to take less dense diets (76). Water content or fibre content can reduce digestibility slightly (170) as well as protract absorption. Lack of dietary fibre has been blamed for diabetes mellitus (182). Mayer has proposed that a major contributor to obesity is a breakdown in energy balancing mechanisms when too little exercise is taken (153). Gastric clearance may be important in this, for exercise (at least if severe enough) can slow gastric emptying (137). Acute slowing by stress might desatiate and contribute to emotional eating.

The standard techniques for determining gastric clearance functions would be difficult to apply in obese but otherwise healthy subjects, and impossible in anorexia nervosa. However, it may be advisable to test carefully the possibility that consistent differences in gastric functions relate to differences in intake, adiposity or glucose tolerance. Unfortunately it is clear from our modelling that quite small differences in absorption rate, if persistently repeated, are sufficient to generate the adaptations and the insidious accumulation of fat that is of concern. A good model of human feeding control would indeed provide an estimate of the size of effect to look for.

Therapy

Modelling in general and the energy-flow theory in particular are likely to have therapeutic applications. Some specific suggestions we made earlier (35) were:

(i) Attribute cachexic anorexia in large part to misinformation of satiety receptors by the rapid output of energy from tissues. Loss of motivation and a will to live may not be a symptom for terminal prognosis, but an involuntary self-starvation which is unnecessarily allowed to tighten into a fatal spiral.

(ii) Use the rush of postabsorptive energy provided by concentrated starch to provide a model satiety experience to train obese subjects or recovering anorexics, in cases where the subject has been shown to be insufficiently controlled by feeding-related sensations.

(iii) Use the formal procedure for acquisition of anticipatory sensory control of energy-induced satiation to improve discriminative self-control of amounts and nutrient densities of food taken by obese subjects.

A possibility which can be added is (iv) biofeedback control of gastric clearance, and hence the gastric clearance function, as this is under autonomic control, is subject to emotional influences, and has consequences likely to stimulate afferents - just like the heart. Gastric motility participates in the 1½-2 hr "oral drive" rhythm (68) which may well be a result of conditioning. A noninvasive sensor of gastric motility, reliably indicating current gastric clearance rate, would be needed.

A more general suggestion was (35) that (v) a computer model which predicted both intake and weight changes in man would be of great benefit to behaviour modification. The behavioural and physiological characteristics of an individual client could be read into a general working model. Then the results of simulations could be used to specify a plan of behavioural, nutritional and weight changes which should both minimise the problems arising from physiological

influences and optimise the change in weight. Mahoney (107) has deplored the current tendency to assume without evidence that changes in feeding behaviour such as slower chewing are weight reducing. Therapy often relies on unreliable and little understood mediating reinforcers. It therefore behoves the modifier to use available information on the mechanisms underlying the contingencies between feeding behaviour, food, body events, and the attainment of access to what may be the best reinforcer of all - a tolerable target reduced weight.

REFERENCES

(1) Adair, E. R.; Miller, N. E.; and Booth, D. A. 1968. Effects of continuous intravenous infusion of nutritive substances on consummatory behavior in rats. Commun. behav. Biol. 2: 25-37.

(2) Allison, J., and Castellan, N. J. 1970. Temporal characteristics of nutritive drinking in rats and humans. J. comp. physiol. Psychol. 70: 116-125.

(3) Antelman, S. M., and Szechtman, H. 1975. Tail pinch induces eating in sated rats which appears to depend on nigrostriatal dopamine. Science 189: 731-732.

(4) Armstrong, J. S. 1971. Modelling a grazing system. Proc. Ecol. Soc., Austral. 6: 194-202.

(5) Ball, G. G. 1974. Vagotomy: effect on electrically elicited eating and self-stimulation in the lateral hypothalamus. Science 184: 484-485.

(6) Barnwell, G. M., and Stafford, F. S. 1975. Mathematical model for decision-making neural circuits controlling food intake. Bull. Psychon. Soc. 5: 473-476.

(7) Beatty, W. W.; O'Briant, D. A.; and Vilberg, T. R. 1975. Effects of ovariectomy and estrodiol injections on food intake and body weight in rats with ventromedial lesions. Pharmacol. Biochem. Behav. 3: 539-544.

(8) Bindra, D. 1972. A unified account of classical conditioning and operant training. In Classical Conditioning II: Current Research and Theory, ed. A. H. Black and W. F. Prokasy, pp. 453-481. New York: Appleton-Century-Crofts.

(9) Bliss, D. K.; Sledjeski, M.; and Leiman, A. L. 1971. State dependent choice behavior in the rhesus monkey. Neuropsychologia 9: 51-59.

(10) Bliss, T. V. P.; Burns, B. D.; and Uttley, A. M. 1968. Factors affecting the conductivity of pathways in cerebral cortex. J. Physiol. Lond. 195: 339-359.

(11) Blundell, J. E. 1974. Anorexia drugs, food intake and study of obesity. Nutrition, Lond. 29: 5-18.

(12) Bolles, R. C. 1972. Reinforcement, expectancy, and learning. Psychol. Rev. 79: 394-409.

(13) Booth, D. A. 1972. Caloric compensation in rats with continuous or intermittent access to food. Physiol. Behav. 8: 891-899.

(14) Booth, D. A. 1972. Taste reactivity in starved, ready to eat and recently fed rats. Physiol. Behav. 8: 901-908.

(15) Booth, D. A. 1972. Satiety and behavioral caloric compensation following intragastric glucose loads in the rat. J. comp. physiol. Psychol. 78: 412-432.

(16) Booth, D. A. 1972. Postabsorptively induced suppression of appetite and the energostatic control of feeding. Physiol. Behav. 9: 199-202.

(17) Booth, D. A. 1972. Some characteristics of feeding during streptozotocin-induced diabetes in the rat. J. comp. physiol. Psychol. 80: 238-249.

(18) Booth, D. A. 1972. Conditioned satiety in the rat. J. comp. physiol. Psychol. 81: 457-471.

(19) Booth, D. A. 1972. The effect of variety on appetite. Unpublished MS, University of Sussex.

(20) Booth, D. A. 1972. Acquired sensory preferences for protein in diabetic and normal rats. Physiol. Psychol. 2: 344-348.

(21) Booth, D. A. 1974. Food intake compensation for increase or decrease in the protein content of the diet. Behav. Biol. 12: 31-40.

(22) Booth, D. A. 1977. Prediction of feeding behaviour from energy flows in the rat. In Hunger Models: Computable Theory of Feeding Control, ed. D. A. Booth. London: Academic Press.

(23) Booth, D. A., and Campbell, C. S. 1975. Relation of fatty acids to feeding behaviour: effects of palmitic acid infusions, lighting variation and pent-4-enoate, insulin or propranolol injections. Physiol. Behav. In press.

(24) Booth D. A., and Davis, J. D. 1973. Gastrointestinal factors in the acquisition of oral sensory control of satiation. Physiol. Behav. 11: 23-29.

(25) Booth, D. A., and Jarman, S. P. 1975. Ontogeny and insulin-dependence of the satiation which follows carbohydrate absorption in the rat. Behav. Biol. 15: 159-172.

(26) Booth, D. A., and Jarman, S. P. 1976. Inhibition of food intake in the rat following complete absorption of glucose delivered into the stomach, intestine or liver. J. Physiol., Lond., in press.

(27) Booth, D. A.; Lee, M.; and McAleavey, C. 1976. Acquired sensory control of satiation in man. Br. J. Psychol., in press.

(28) Booth, D. A.; Lovett, D.; and McSherry, G. M. 1972. Post-ingestive modulation of the sweetness preference gradient in the rat. J. comp. physiol. Psychol. 78: 485-512.

(29) Booth, D. A., and Pain, J. F. 1970. Effects of a single insulin injection on approaches to food and on the temporal pattern of feeding. Psychon. Sci. 21: 17-19.

(30) Booth, D. A., and Simson, P. C. 1971. Food preferences acquired by association with variations in amino acid nutrition. Quart. J. exp. Psychol. 23: 135-145.

(31) Booth, D. A., and Simson, P. C. 1974. Taste aversion induced by an histidine-free amino acid load. Physiol. Psychol. 2: 349-351.

(32) Booth, D. A., and Simson, P. C. 1972. Unpublished data.

(33) Booth, D. A.; Stoloff, R.; and Nicholls, J. 1974. Dietary flavor acceptance in infant rats established by association with effects of nutrient composition. Physiol. Psychol. 2: 313-319.

(34) Booth, D. A., and Toates, F. M. 1974. A physiological control theory of food intake in the rat: Mark 1. Bull. Psychon. Soc. 3: 442-444.

(35) Booth, D. A.; Toates, F. M.; and Platt, S. V. 1976. Control system for hunger and its implications in animals and man. In Hunger: Basic Mechanisms and Clinical Implications, ed. D. Novi, W. Wyrwicka and G. A. Bray, pp. 127-142. New York: Raven Press.

(36) Borbely, A. A., and Huston, J. P. 1974. Effects of two-hour light-dark cycles on feeding, drinking and motor activity of the rat. Physiol. Behav. 13: 795-802.

(37) Brobeck, J. R. 1965. Exchange, control and regulation. In Physiological Controls and Regulation, ed. W. S. Yamomoto and J. R. Brobeck, pp. 1-13. Philadelphia: Saunders.

(38) Bruch, H. 1973. Eating Disorders: Obesity, Anorexia Nervosa and the Person Within. New York: Basic Books.

(39) Buttorfield, W. J. H.; Abrams, M. E.; Sells, R. A.; Starky, G.; and Whichelow, M. J. 1966. Insulin sensitivity of the human brain. Lancet i: 557-560.

(40) Chance, M. R. A., and Mead, A. P. 1955. Competition between feeding and investigation in the rat. Behaviour 8: 174-182.

(41) Coddington, R. D., and Bruch, H. 1970. Gastric perceptivity in normal, obese and schizophrenic subjects. Psychosomatics 11: 571-579.

(42) Collier, G.; Hirsch, E.; and Hamlin, P. H. 1972. The ecological determinants of reinforcement in the rat. Physiol. Behav. 9: 705-716.

(43) Das, T. K., and Waterlow, J. C. 1974. The rate of adaption of urea cycle enzymes, aminotransferases and glutamate dehydrogenase to changes in dietary protein intake. Br. J. Nutr. 32: 353-373.

(44) Davis, J. D.; Collins, B. J.; and Levine, M. W. 1975. Peripheral control of drinking: gastro-intestinal filling as a negative feedback signal, a theoretical and experimental analysis. J. comp. physiol. Psychol., in press.

(45) Davis, J. D.; Collins, B. J.; and Levine, M. W. 1977. A control model of nutritive drinking. In Hunger Models: Computable Theory of Feeding Control, ed. D. A. Booth. London: Academic Press.

(46) Drew, G. C. 1937. The recurrence of eating in rats after apparent satiation. Proc. Zool. Soc., Lon. 107: 95-106.

(47) Duclaux, R.; Feisthauer, J.; and Cabanac, M. 1973. Effets du repas sur l'agrément d'odeurs alimentaires et non alimentaires chez l'homme. Physiol. Behav. 10: 1029-1034.

(48) Eastman, C., and Booth, D. A. 1975. Reversal tests of acquired olfactory control of meal size in the rat. Unpublished data, University of Birmingham.

(49) Edelsten, P., and Newton, J. E. 1975. A simulation model of intensive lamb production from grass. Tech. Rep. 17, 49 pp. Grassland Research Institute, Hurley, Berks.

(50) Epstein, A. N. 1971. The lateral hypothalamic syndrome: its implications for the physiological psychology of hunger and thirst. Prog. Physiol. Psychol. 4: 263-317.

(51) Fitzsimons, J. T., and Le Magnen, J. 1969. Eating as a regulatory control of drinking in the rat. J. comp. physiol. Psychol. 67: 273-283.

(52) Flatt, J. P.; Blackburn, G. L.; Randers, G.; and Stanbury, J. B. 1974. Effects of ketone body infusion on hypoglycemic reaction in postabsorptive dogs. Metabolism 23: 151-158.

(53) Garcia, J.; Hankins, W. G.; and Rusiniak, K. W. 1974. Behavioral regulation of the milieu interne in man and rat. Science 185: 824-832.

(54) Garrow, J. S. 1974. Energy Balance and Obesity in Man. Amsterdam: North-Holland.

(55) Geertsema, S. P. 1973. Ontwikkeling analyse en toepassingen van enige modellen der regulatie van voedselopname. Unpublished Ph.D. thesis, University of Groningen.

(56) Geertsema, S. P., and Reddingius, H. 1974. Preliminary considerations in the simulation of behaviour. In Motivational Control Systems Analysis, ed. D. J. McFarland, pp. 355-405. London: Academic Press.

(57) Geiger, A. 1958. Correlation of brain metabolism and function by use of a brain perfusion method in situ. Physiol. Rev. 38: 1-20.

(58) Gold, R. M. 1970. Hypothalamic hyperphagia: males get just as fat as females. Physiol. Psychol. 71: 347-356.

(59) Gold, R. M. 1975. Hypothalamic hyperphagia despite imposed diurnal or nocturnal feeding and drinking rhythms. Physiol. Behav. 14: 861-866.

(60) Graff, H., and Stellar, E. 1962. Hyperphagia, obesity and finickiness. J. comp. physiol. Psychol. 55: 418-424.

(61) Grastyán, E., and Vereczkei, L. 1974. Effects of spatial separation of the conditioned signal from the reinforcement: a demonstration of the conditioned character of the orienting response or the orientational character of conditioning. Behav. Biol. 10: 121-146.

(62) Griffith, G. H.; Owen, G. M.; Campbell, P. H.; and Shields, R. 1968. Gastric emptying in health and gastroduodenal disease. Gastroenterology 54: 1-7.

(63) Griggs, R. C., and Stunkard, A. J. 1964. The interpretation of gastric motility. II. Sensitivity and bias in the perception of motility. Arch. gen. Psychiat. 11: 82-89.

(64) Grossman, S. P. 1975. Role of the hypothalamus in the regulation of food and water intake. Psychol. Rev. 82: 200-224.

(65) Hall, W. G. 1974. Remote stomach clamp to evaluate oral and gastric controls of drinking in the rat. Physiol. Behav. 11: 897-898.

(66) Harper, A. E., and Spivey, H. E. 1958. Relationship between food intake and osmotic effect of dietary carbohydrate. Am. J. Physiol. 193: 483-487.

(67) Harvey, G. R. 1969. Regulation of energy balance. Nature 222: 629-631.

(68) Hiatt, J. F., and Kripke, D. F. 1975. Ultradian rhythms in waking gastric activity. Psychosom. Med. 37: 320-325.

(69) Hill, S. W. 1974. Eating responses of humans during dinner meals. J. comp. physiol. Psychol. 86: 652-657.

(70) Hirsch, J. 1972. Discussion. Adv. psychosom. Med. 7: 229-242.

(71) Hogan, J. A. 1975. Development of food recognition in young chicks: III. Discrimination. J. comp. physiol. Psychol. 89: 95-104.

(72) Holman, E. W. 1973. Temporal properties of gustatory spontaneous alternation in rats. J. comp. physiol. Psychol. 85: 536-539.

(73) Holman, G. L. 1969. Intragastric reinforcement effect. J. comp. physiol. Psychol. 69: 432-441.

(74) Hopkins, A. 1966. The pattern of gastric emptying: a new view of old results. J. Physiol., Lond. 182: 144-149.

(75) Hunt, J. N. 1974. Personal communication.

(76) Hunt, J. N.; Cash, R.; and Newland, P. 1975. Energy density of food, gastric emptying, and obesity. Lancet ii: 905-906.

(77) Hunt, J. N., and Knox, M. T. 1968. Regulation of gastric emptying. In Handbook of Physiology, Alimentary Canal, Vol. 4, Motility, ed. C. F. Code and W. Heidel, pp. 1917-1935. Washington, D.C.: Amer. Physiol. Soc.

(78) Hunt, J. N., and Stubbs, D. F. 1975. The volume and energy content of meals as determinants of gastric emptying. J. Physiol. Lond. 245:

(79) Huston, J. P. 1975. Classical conditioning of consumatory behaviour. In Control Mechanisms of Drinking, ed. G. Peters, J. T. Fitzsimons and L. Peters-Haefel:, pp. 165-172. Berlin: Springer-Verlag.

(80) Jacobs, H. L. 1964. Observations on the ontogeny of saccharin preference in the neonate rat. Psychon. Sci. 1: 105-106.

(81) Jacobs, H. L. 1964. Evaluation of the osmotic effects of glucose loads on food satiation. J. comp. physiol. Psychol. 57: 309-310.

(82) Jacobs, H. L., and Sharma, K. N. 1969. Taste versus calories: sensory and metabolic signals in the control of food intake. Ann. N.Y. Acad. Sci. 157: 1084-1112.

(83) James, A. H. 1961. The Physiology of Gastric Digestion. London: Arnold.

(84) Johansson, C. 1975. Studies of gastrointestinal interactions. VIII. Characteristics in the absorption pattern of sugar, fat and protein from composite meals in man. A quantitative study. Scand. J. Gastroent. 10: 1-19.

(85) Jordan, H. A.; Moses, H.; MacFayden, B. V.; and Dudrick, S. J. 1974. Hunger and satiety in humans during parenteral hyperalimentation. Psychosom. Med. 36: 144-155.

(86) Keesey, R. E.; Boyle, P. C.; Kemnitz, J. W.; and Mitchel, J. S. 1976. Lateral hypothalamic determination of the body weight set-point. In Hunger: Basic Mechanisms and Clinical Implications, ed. D. Novin, W. Wyrwicka and G. A. Bray. New York: Raven Press.

(87) Kennedy, G. C. 1953. The role of depot fat in the hypothalamic control of food intake in the rat. Proc. Roy. Soc., Lond., B. 140: 578-592.

(88) Krane, R. V., and Wagner, A. R. 1975. Taste aversion with a delayed shock US: implications for the "generality of the laws of learning". J. comp. physiol. Psychol. 88: 882-889.

(89) Krebs, J. 1973. Behavioral aspects of predation. In Perspectives in Ethology, ed. P. P. G. Bateson and H. Kloppfer. New York: Plenum Press.

(90) Krieckhaus, E. E., and Wolf, G. 1968. Acquisition of sodium by rats: interaction of innate mechanisms and latent learning. J. comp. physiol. Psychol. 65: 197-201.

(91) Kuhn, T. S. 1962. The Structure of Scientific Revolutions. Chicago: Aldine.

(92) Lasser, R. B.; Bond, T. H.; and Levitt, M. D. 1975. The role of intestinal gas in functional abdominal pain. New Engl. J. Med. 293: 524-526.

(93) Le Magnen, J. 1956. Hyperphagie provoquée chez le rat blanc par alteration due mécanisme de satiété peripherique. C.R. Soc. Biol. 150: 32-35.

(94) Le Magnen, J. 1956. Role de l'odeur ajoutée au regime dans le régulation quantitative à court terme de la prise alimentaire chez le rat blanc. C.R. Soc. Biol. 150: 136-139.

(95) Le Magnen, J. 1956. Effets sur la prise alimentaire du rat blancs des administrations post-prandiales d'insuline et le mécanisme des appétits caloriques. J. Physiol. Paris 48: 789-802.

(96) Le Magnen, J. 1959. Effets des administrations post-prandiales de glucose sur l'établissement des appétits. C.R. Soc. Biol. 153: 212-215.

(97) Le Magnen, J. 1961. Effets d'une pluralité de stimuli alimentaire sur le determinisme quantitatif de l'ingestion chez le rat blanc. Arch. Sci. Physiol. 14: 411-419.

(98) Le Magnen, J. 1963. La facilitation différentielle des réflexes d'ingestion par l'odeur alimentaire. C.R. Soc. Biol. 157: 1165-1170.

(99) Le Magnen, J. 1971. Advances in studies on the physiological control and regulation of food intake. Prog. Physiol. Psychol. 4: 204-261.

(100) Le Magnen, J., and Devos, M. 1970. Metabolic correlates of meal onset in the free food intake of rats. Physiol. Behav. 5: 805-814.

(101) Le Magnen, J.; Devos, M.; Gaudillière, J.-P.; Louis-Sylvestre, J.; and Tallon, S. 1973. Role of a lipostatic mechanism in regulation by feeding of energy balance in rats. J. comp. physiol. Psychol. 84: 1-23.

(102) Le Magnen, J., and Tallon, S. 1966. La périodicité spontanée de la prise d'aliments ad libitum du rat blanc. J. Physiol. Paris 58: 323-349.

(103) Le Magnen, J., and Tallon, S. 1968. L'effet du jeûne préable sur les caracteristiques temporelles de la prise d'aliments chez le rat. J. Physiol. Paris 60: 143-154.

(104) Leon, J. 1976. Life histories as adaptive strategies. J. theor. Biol., in press.

(105) Leung, P. M. B., and Rogers, Q. R. 1969. Food intake: regulation by amino acid pattern. Life Sci. 8: 1-9.

(106) Leung, P. M. B., and Rogers, Q. R. 1973. Effect of amygdaloid lesions on dietary intake of disproportionate amounts of amino acids. Physiol. Behav. 11: 221-226.

(107) Mahoney, M. J. 1975. Fat fiction. Behav. Ther. 6: 416-418.

(108) Mather, P., and Booth, D. A. 1977. A prototype computer model of human appetite, growth and obesity. In Hunger Models: Computable Theory of Feeding Control, ed. D. A. Booth. London: Academic Press.

(109) McCleary, R. A. 1953. Taste and post-ingestion factors in specific-hunger behavior. J. comp. physiol. Psychol. 46: 411-421.

(110) McFarland, D. J. 1971. Feedback Mechanisms in Animal Behaviour. London: Academic Press.

(111) McFarland, D. J. (ed.) 1974. Motivational Control Systems Analysis. London: Academic Press.

(112) McFarland, D. J., and Lloyd, I. H. 1973. Time shared feeding and drinking. Quart. J. exp. Psychol. 25: 48-61.

(113) McFarland, D. J., and Sibley, R. M. 1975. The behavioural common path. Phil. Trans. Roy. Soc., Lond. B 270: 265-293.

(114) Mears, G. J., and Mendel, V. E. 1974. Correlation of food intake in lambs with adipocyte glucose metabolism and NEFA release. J. Physiol., Lond. 240: 625-637.

(115) Miller, N. E. 1965. Chemical coding of behavior in the brain. Science 148: 328-338.

(116) Miller, N. E. 1973. Commentary. In Brain Stimulation and Motivation, ed. E. S. Valenstein, pp. 53-68. Glenview, Ill.: Scott, Foresman.

(117) Mineka, S. 1975. Some new perspectives on conditioned hunger. J. comp. physiol. Psychol. 104: 134-148.

(118) Mok, A. C. S., and Mogenson, G. J. 1974. Effects of electrical stimulation of the lateral habenular nucleus and lateral hypothalamus on unit activity in upper brain-stem. Brain Res. 78: 425-435.

(119) Monteiro, L. S. 1972. The control of appetite in lactating cows. Anim. Prod. 14: 263-281.

(120) Morgane, P. J. 1969. The function of the limbic and rhinic forebrain-limbic midbrain systems and reticular formation in the regulation of food and water intake. Ann. N.Y. Acad. Sci. 157: 806-848.

(121) Morrison, S. D. 1975. Feeding analogues. Nature 255: 169.

(122) Nicolaidis, S. 1974. A possible molecular basis of regulation of energy balance. XXVI Int. Cong. Physiol. Sci.: Food and Fluid Intake, Jerusalem.

(123) Noda, K. 1975. Possible effect of blood ammonia on food intake of rats fed amino acid imbalanced diets. J. Nutr. 105: 508-516.

(124) Norgren, R. 1975. Gustatory afferents to the ventral forebrain. Brain Res. 81: 285-295.

(125) Oatley, K. 1973. Simulation and theory of thirst. In The Neuropsychology of Thirst, ed. A. N. Epstein, J. Stellar and H. R. Kissileff, pp. 199-223. New York: Winston.

(126) Oatley, K. 1974. Circadian rhythms and representations of the environment in motivational systems. In Motivational Control Systems Analysis, ed. D. J. McFarland, pp. 427-459. London: Academic Press.

(127) Oatley, K., and Toates, F. M. 1969. The passage of food through the gut of rats and its uptake of fluid. Psychon. Sci. 16: 225-226.

(128) Oomura, Y.; Sugimori, M.; Nakamura, T.; and Yamada, Y. 1975. In Neural Integration of Physiological Mechanisms and Behaviour, ed. G. J. Mogenson and F. R. Calaresu, pp. 375-395. Toronto: University of Toronto Press.

(129) Pain, J. F., and Booth, D. A. 1968. Toxiphobia to odors. Psychon. Sci. 10: 363-364.

(130) Panksepp, J. 1973. Reanalysis of feeding patterns in the rat. J. comp. physiol. Psychol. 82: 78-94.

(131) Panksepp, J. 1975. Mathematical analysis of energy regulatory patterns of normal and diabetic rats. J. comp. physiol. Psychol. in press.

(132) Panksepp, J., and Pilcher, C. W. T. 1973. Evidence for an adipokinetic mechanism in ventromedial hypothalamus. Experientia 29: 793-794.

(133) Petersen, S. A. 1975. Gonadal hormones and feeding behaviour in the mouse. Unpublished Ph.D. thesis, University of Edinburgh.

(134) Pilcher, C. W. T.; Jarman, S. P.; and Booth, D. A. 1974. The route of glucose to the brain from food in the mouth of the rat. J. comp. physiol. Psychol. 87: 56-61.

(135) Powley, T. L., and Opsahl, C. A. 1974. Ventromedial hypothalamic obesity abolished by subdiaphragmatic vagotomy. Am. J. Physiol. 226: 25-30.

(136) Rafaelson, O. J. 1967. Insulin action on the central nervous system. Acta med. Scand., Suppl. 476: 75-84.

(137) Ramsbottom, N., and Hunt, J. N. 1974. Effect of exercise on gastric emptying and gastric secretion. Digesion 10: 1-8.

(138) Rescorla, R. A., and Wagner, A. R. 1972. A theory of classical conditioning. In Classical conditioning II, ed. A. Black and W. F. Prokasy. New York: Appleton-Century-Crofts.

(139) Revusky, B. T. 1970. Failure to support the hypothesis that eating is anticipatory of need. Psychol. Rep. 27: 199-205.

(140) Revusky, S. 1974. Retention of a learned increase in the preference for a flavored solution. Behav. Biol. 11: 121-125.

(141) Rezek, M.; Vanderweele, D. A.; and Novin, D. 1975. Stages in the recovery of feeding following vagotomy in rabbits. Behav. Biol. 14: 75-84.

(142) Rolls, B. J. 1975. Interaction of hunger and thirst in rats with lesions of the preoptic area. Physiol. Behav. 14: 537-543.

(143) Rolls, E. T. 1974. The neural basis of brain-stimulation reward. Prog. Neurobiol. 3: 71-160.

(144) Rowland, N. 1975. Personal communication.

(145) Rowland, N. E., and Antelman, S. M. 1976. Stress-induced hyperphagia and obesity in rats: a possible model for understanding human obesity. Science, in press.

(146) Rowland, N.; Meile, M. J.; Nicolaïdis, S. 1973. Action inadéquate des apports parentéraux sur l'insulino-sécrétion et sur le contrôle du comportement alimentaire chez le rat. C.R. Acad. Sci. 277: 1783-1786.

(147) Rozin, P. 1967. Specific aversions as a component of specific hungers. J. comp. physiol. Psychol. 64: 237-242.

(148) Rozin, P., and Kalat, J. W. 1971. Specific hungers and poison avoidance as adaptive specializations of learning. Psychol. Rev. 78: 459-486.

(149) Rusnak, M. 1971. Hepatic receptors and the neurophysiological mechanisms controlling feeding behavior. Neurosci. Res. 4: 213-282.

(150) Rusnak, M. 1976. A "conceptual" equation of intake control. In Hunger: Basic Mechanisms and Clinical Implications, ed. D. Novin, W. Wyrwicka and G. A. Bray. New York: Raven Press.

(151) Rusnak, M. 1977. Semiquantitative simulation of food intake control and weight regulation. In Hunger Models: Computable Theory of Feeding Control, ed. D. A. Booth. London: Academic Press.

(152) Sahibzada, A. J. 1974. Personal communication.

(153) Saltzer, C. C., and Mayer, J. 1970. An effective weight control program in a public school system. Am. J. publ. Health 60: 679-689.

(154) Shettleworth, S. J. 1975. Reinforcement and the organization of behavior in golden hamsters: hunger, environment, and food reinforcement. J. exp. Psychol. Anim. Behav. Proc. 104: 56-87.

(155) Sibly, R. M. 1975. How deficit and incentive determine feeding tendency. Anim. Behav. 23: 437-447.

(156) Sibly, R. M., and McFarland, D. 1976. On the fitness of behavior sequences. Am. Naturalist, in press.

(157) Siegel, J. M. 1975. REM sleep predicts subsequent food intake. Submitted for publication.

(158) Simson, P. C., and Booth, D. A. 1975. Subcutaneous release of amino acid loads on food and water intakes in the rat. Physiol. Behav. 14: 329-336.

(159) Simson, P. C., and Booth, D. A. 1974. Olfactory conditioning by association with histidine-free or balanced amino acid loads. Quart. J. exp. Psychol. 25: 354-359.

(160) Simson, P. C., and Booth, D. A. 1974. Dietary aversion established by a deficient load: specificity to the amino acid omitted from a balanced mixture. Pharmacol. Biochem. Behav. 2: 481-485.

(161) Smith, C. V. J. 1972. Hypothalamic glucoreceptors - the influence of gold thioglucose implants in the ventromedial and lateral hypothalamic areas of normal and diabetic rats. Physiol. Behav. 9: 391-396.

(162) Smith, G. P. 1974. Adrenal hormones and emotional behaviour. In Progress in Physiological Psychology 5, ed. J. M. Sprague and E. Stellar, pp. 330-345. New York: Academic Press.

(163) Smith, G. P., and Gibbs, J. 1976. What the gut tells the brain about feeding behavior. In Dahlem Workshop on Appetite and Food Intake, ed. T. Silverstone. Berlin: Dahlem Konferenzen.

(164) Smith, G. P; Gibbs, J.; and Young, R. C. 1974. Cholecystokinin and intestinal satiety in the rat. Fed. Proc. 33: 1146-1149.

(165) Smith, M.; Pool, R.; and Weinberg, H. 1959. The effect of peripheral induced shifts in water balance on eating. J. comp. physiol. Psychol. 52: 289-293.

(166) Smith, U. 1970. Effects of glucose and insulin on lipolysis rates in human fat cells of different sizes. FEBS Letters 11: 8-10.

(167) Smutz, E. R.; Hirsch, E.; and Jacobs, H. L. 1975. Caloric compensation in hypothalamic obese rats. Physiol. Behav. 14: 305-309.

(168) Snowdon, C. T. 1970. Gastrointestinal sensory and motor control of food intake. J. comp. physiol. Psychol. 71: 68-76.

(169) Soulairac, A. 1958. Les régulations psycho-physiologiques de la faim. J. Physiol. Paris 50: 710-783.

(170) Southgate, D. A. T., and Durnin, J. V. G. A. 1970. Calorie conversion factors. An experimental reassessment of the factors used in the calculation of the energy value of human diets. Br. J. Nutr. 24: 517-535.

(171) Spiegel, T. A. 1975. Caloric regulation of food intake in man. J. comp. physiol. Psychol. 88: 24-37.

(172) Steffens, A. B. 1969. Rapid absorption of glucose in the intestinal tract of the rat after ingestion of meal. Physiol. Behav. 4: 829-832.

(173) Steffens, A. B. 1975. Influence of reversible obesity on eating behavior, blood glucose, and insulin in the rat. Am. J. Physiol. 228: 1738-1744.

(174) Strubbe, J. H. 1975. Insulin, glucose and feeding behaviour in the rat: a reappraisal of the glucostatic theory. Ph.D. thesis, University of Groningen.

(175) Szabo, O., and Szabo, A. J. 1975. Studies on the nature and mode of action of the insulin-sensitive glucoreceptor in the central nervous system. Diabetes 24: 328-336.

(176) Taylor, C. R.; Schmidt-Nielsen, K.; and Raab, J. L. 1970. Scaling of energetic cost of running to body size in mammals. Am. J. Physiol. 219: 1104-1107.

(177) Teitelbaum, P. 1967. Motivation and control of food intake. In Handbook of Physiology, Alimentary Canal, Vol. 1, Food and Water Intake, ed. C. F. Code and W. Heidel, pp. 319-335. Washington, D.C.: American Physiological Society.

(178) Thomas, G. J.; Hostetter, G.; and Barker, D. J. 1968. Prog. Physiol. Psychol. 2: 230-311.

(179) Toates, F. M. 1975. Control Theory in Biology and Experimental Psychology. London: Hutchinson Educational.

(180) Toates, F. M., and Booth, D. A. 1974. Control of food intake by energy supply. Nature 251: 710-711.

(181) Toates, F. M., and Oatley, K. 1970. Computer simulation of thirst and water balance. Med. biol. Eng. 8: 71-87.

(182) Trowell, H. C. 1975. Dietary-fiber hypothesis of the etiology of diabetes mellitus. Diabetes 24: 762-765.

(183) Uttley, A. M. 1975. The Informon in classical conditioning. J. theor. Biol. 45: 355-376.

(184) Wagner, A. R.; Rudy, J. W.; Whitlow, J. W. 1973. Rehearsal in animal conditioning. J. exp. Psychol. 97: 407-426.

(185) Wampler, R. S., and Gier, H. T. Continuing gonadal function in rats with ventromedial hypothalamic area lesions. J. comp. physiol. Psychol. 87: 831-839.

(186) Webster, A. J. F. 1974. Personal communication.

(187) Weiskrantz, L. 1975. Problems and progress in physiological psychology. Br. J. Psychol. 64: 511-520.

(188) Wiepkema, P. R. 1971. Positive feedbacks at work during feeding. Behaviour 39: 266-273.

(189) Wittgenstein, L. 1953. Philosophical Investigations. Oxford: Blackwells.

(190) Wolgin, D. L.; Cytawa, J.; and Teitelbaum, P. 1976. The role of activation in the regulation of food intake. In Hunger: Basic Mechanisms and Clinical Implications, ed. D. Novin, W. Wyrwicka and G. A. Bray. New York: Raven Press.

(191) Woods, S. C.; Decke, E.; and Vaselli, J. R. 1974. Metabolic hormones and regulation of body weight. Psychol. Rev. 81: 26-43.

(192) Wright, P., and Crow, R. A. 1974. Menstrual cycle-effect on sweetness preference in women. Horm. Behav. 4: 387-395.

(193) Wunder, B. A. 1975. A model for estimating metabolic rate of active or resting animals. J. theor. Biol. 49: 345-354.

(194) Young, P. T. 1967. Palatability: the hedonic response to foodstuffs. In Handbook of Physiology, Alimentary Canal, Vol. 1, Food and Water Intake, ed. C. F. Code. Washington, D.C.: Amer. Physiol. Soc.

(195) Zahler, L. P., and Harper, A. E. 1972. Effects of dietary amino-acid pattern on food preference behavior of rats. J. comp. physiol. Psychol. 81: 155-161.

(196) Zeeman, E. C. 1972. A catastrophe machine. In Towards a Theoretical Biology 4, ed. C. H. Waddington, pp. 276-282. Edinburgh: University Press.

(197) Zepelin, H., and Rechtschaffen, A. 1974. Mammalian sleep, longevity and energy metabolism. Brain Behav. Evol. 10: 425-470.

(198) Zuckerman, D. C. 1975. Motivational cues as determiners of stimulus control in rats. Anim.Learn.Behav.3:250-256.

Report of the Dahlem Workshop on
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Berlin 1975, December 8 to 12

Trevor Silverstone, Editor

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Dahlem Konferenzen

Dahlem Konferenzen

Founder and Year:
Dahlem Konferenzen was founded in 1974 and is supported by the Stifterverband für die Deutsche Wissenschaft, the science foundation of German industry, trade, and commerce, in cooperation with the Deutsche Forschungsgemeinschaft, the German organization for promoting fundamental research.

Purpose:
To promote the interdisciplinary exchange of scientific information and ideas and to stimulate international cooperation in research.

Program:
To plan and organize workshops on topics which are of international interest and suitable for an interdisciplinary approach; to explore different types of scientific conferences, and to disseminate the results.

The Dahlem Workshop Structure:
The workshop is set up on an interdisciplinary basis with plenary and small group discussions. Lectures are not presented.
A number of participants are asked to write background papers. These papers provide a review of the field rather than a report on individual work. They are circulated to all participants 4 weeks before the meeting to establish a basis for the discussions.
All participants are requested to read these papers and formulate written questions to them before the meeting.
The workshop begins with plenary discussion of the background papers based on the questions submitted by the participants.
The participants then divide into small discussion groups of 8 to 10 members.
Each group prepares a report reflecting the essential points of its discussion on current knowledge in the field and containing suggestions for further research. The reports are distributed to all participants during the meeting and are discussed in plenum.

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