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Set Points, Settling Points, and the Control of Body Weight[1]

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WIRTSHAFTER, D. AND J D. DAVIS. *Set points, settling points, and the control of body weight.* PHYSIOL. BEHAV. 19(1) 75–78, 1977. — Recently a number of investigators have suggested that body weight may be controlled by a neural system which contains a reference or set point. The finding that the body weight level which animals will defend can be altered by lesions of the lateral and ventromedial hypothalamus has been taken to provide support for this claim. In this paper we describe a simple feedback control model which contains no set point, and yet is able to account in full for these and other data which have been cited in support of the existence of a body weight set point Since such a model exists it appears to be unnecessary and unparsimonious to introduce the concept of a neural set point to explain the fact that body weight maintains a relatively constant value which is defended against certain types of challenges. Constancy and defense of body weight are at best only *prima facie* evidence for the existence of a neural set point controlling body weight

Set point Body weight control theory Lipostat hypothesis Feeding Homeostasis VMH LH

IN RECENT YEARS the application of control theory to the problems of physiology [27] and behavior [1, 6, 15, 18, 24, 30] has become widespread. The increasing interest in the use of feedback models to further our understanding of the control of behavior seems to be justified in part because the consequences of what organisms do very often feed back in some sense to alter ongoing or subsequent behavior Furthermore, control theory provides a way to analyze in a logical and quantitative manner complicated systems that are influenced by a multiplicity of variables often operating simultaneously. Toates and Oatley [31] have shown, for example, that the many variables which control water intake in the rat can be organized by control theory techniques to provide a remarkably comprehensive model of thirst in this animal.

The growing interest in the use of control theory to analyze the physiological substrates of behavior has prompted a number of investigators to suggest that body weight, or some closely related quantity such as total lipid volume, may be regulated by means of a set point control system [4, 7, 13, 19, 20, 22, 28, 32]. Indeed, this conception of weight control has become so popular that it is put forward as established fact in at least one introductory psychology text [2]. The defining characteristic of such a system is that it contains a reference point against which the current state of the organism is compared Deviations from the set point generate an error signal which activates the system to correct the deviation. The effect of such a control system is to maintain a relatively constant value of the controlled quantity in the face of disturbances imposed by the environment. It is natural, therefore, when investigating homeostatic systems which adjust to disturbances by making appropriate corrections, to assume that the adjustments are made in response to an error signal indicating deviation from the desired state.

In spite of the popularity of this notion there is a real question concerning its value in furthering our understanding of the control of body weight. Postulating the existence of a neural set point in order to account for the constancy of body weight does not explain much; it merely assigns to the central nervous system (CNS) just that property needed to account for body weight constancy Furthermore, the introduction of such a concept to explain one set of facts creates difficulty in explaining others. For example, it is well known that rodents gain an enormous amount of weight before hibernation [11], that many species of birds increase their fat stores tremendously prior to migration [21], and that females of many species increase body weight during pregnancy [32] It is also well known that rats can be made obese simply by offering them a very palatable high fat diet [16]. To explain these phenomena within the context of a set point model, one would have to assume either that the set point is labile or that it becomes inoperative under certain conditions such as the availability of a high fat diet Of course, either or both of these assumptions may be correct, but skepticism begins

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to develop as the hypothetical set point begins to acquire just that amount of variability which is necessary to explain observed variability in body weight

One reason for the popularity of the set point concept is that it is a plausible and convenient way to account for the maintenance of a stable body weight Plausibility and convenience aside, however, the fundamental question is is a set point necessary to explain the evidence which has been cited in support of its existence? We show here that it is not, since a simple feedback model without a set point can be constructed which can explain all of the evidence which has been cited in support of the existence of a CNS body weight set point Given that this is the case, it becomes clear that those who wish to argue for the existence of a neural set point for body weight will have to provide more direct evidence for it than body weight stability Let us now consider evidence which has been used to support the idea of a set point and see how well an alternate model can explain it

Some of the most convincing support for the existence of a set point for body weight comes from the studies of Keesey and his associates [3, 12, 13, 17, 25] Powley and Keesey [25] found that following small lateral hypothalamic (LH) lesions rats maintain their body weight at lower than normal levels and will defend this lowered weight in the face of various regulatory challenges For example, if the body weight of lesioned animals is further decreased through deprivation or increased through force feeding, these subjects will, upon being returned to ad lib feeding conditions, adjust their food intake so as to regain their previous, postlesioning weight [13] In the most dramatic of these experiments, Powley and Keesey [25] found that rats starved preoperatively to weights below those maintained by LH lesioned animals actually became hyperphagic and gained weight when allowed to feed freely following surgery The hyperphagia continued until the animals reached a new subnormal body weight, at which they stabilized When dietary palatability and caloric density were manipulated, LH and control rats showed almost parallel adjustments in body weight

From these elegant studies Keesey *et al* [13] concluded, "a direct or primary effect of LH lesions is to lower the set point for body weight " If it is granted that hypothalamic lesions can adjust a neural set point, it follows that there must normally exist such a set point and that the LH must somehow be involved in its functioning Although these authors admit that damage to sensory or motor systems might result in lowered weight, it is apparently assumed that such damage could not alter the level at which body weight is actively defended Thus the conclusion of Keesey and his coworkers rests on the assumption that only by altering the set point of the body weight control system could the weight level which the system defends be altered

Let us now consider an alternative model for body weight control Let us suppose that an animal's feeding mechanism is activated by sensory stimuli arising from available food, which we will represent by the letter S, and inhibited by a feedback signal which is proportional to body weight which we will represent by the letter W A control system incorporating these assumptions is shown in Fig 1

In this model, H and G are both constants of proportionality H represents the weighting given to a signal which depends upon the lipid content of the animal's body Although such a signal has not yet been identified, any type

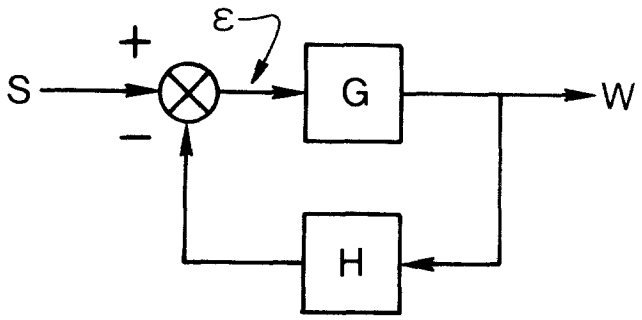

FIG. 1. Diagram of a simple body weight control model which contains no set point See text for details

of system capable of controlling body lipid content must be able to monitor this variable G reflects the functioning of a system which produces, in proportion to its input, ϵ, a particular body weight The elements symbolized by G would thus have to contain, among other things, mechanisms for the short and long-term control of intake G is sometimes known as the forward gain of the system, and H the feedback gain

For simplicity we will ignore the possible dynamics of the model and consider only predictions it makes as to steady state weight Since the output from any box in the diagram is simply the input to it multiplied by the parameter in the box, we can derive a transfer function for this system which will describe how the output of the system, W (body weight), changes with the changes in the input S and changes in the parameters G and H

Thus

$$\epsilon = S - WH$$

$$W = \epsilon G$$

by substitution,

$$W = (S - WH)\, G$$

rearranging,

$$W + GWH = GS$$

and,

$$W = \frac{GS}{1 + GH} \qquad (1)$$

This last formula [1] is the transfer function for the model illustrated in Fig 1 It describes the control of body weight (W) in terms of sensory input and the forward and feedback gain of the system

The value which W assumes is the predicted steady state weight of an organism whose body weight is controlled by the system shown in Fig. 1. We call the value which W takes the settling point of the output of the system, since any change in the values of S, G, or H will alter the value of W and cause it to settle at a new value. Some authors (e.g , [32]) have used the term set point to describe the level at which animals maintain their body weights. We prefer the term settling point since this term is neutral with respect to

the way in which stability is achieved, which may or may not be by means of a neural set point. Furthermore, it avoids the possible confusion which can result from using the same term to refer to both the input and the output of the same system

Consider now the implications of this formula for the control of body weight; it indicates that given constant sensory properties of a diet and constant gains G and H, body weight will be constant Suppose that the effect of a LH lesion were either to lower G or raise H. Then body weight would be lowered to a new settling point. If a lesioned animal which had achieved this new level were deprived, causing W to fall below its settling point determined by the current values of G and H, then were food to be offered again, the animal's weight would increase to predeprivation levels. This is exactly the result which has been reported by Keesey *et al* [13]

The model predicts that increasing the palatability of the food, i e , increasing S, will increase body weight, and decreasing S will decrease body weight. Furthermore it predicts that, if LH lesions affect G and H as discussed above, percentage weight changes for lesioned and control animals in response to altered dietary palatability should be identical This is the effect which Powley and Keesey [25] and Keesey and Boyle [12] have reported

Suppose further that ventromedial hypothalamic (VMH) lesions have opposite effects on the system, that is they either increase G or decrease H Under either or both of these conditions body weight would settle at a new and higher level If a lesioned animal which had achieved this new level were deprived, causing W to fall below its settling point, then were food to be offered again, the animal's weight would increase until the original high level was reached This is the result reported by Hoebel and Teitelbaum [8] using VMH lesioned animals. Again, without the introduction of a set point notion, the model predicts that body weight would be defended. It is interesting to note that the model also predicts that as dietary palatability is lowered towards zero, the weight of normal and VMH lesioned animals will converge to a common value, a result reported by Sclafani, Springer and Kluge [29], and one which is difficult to predict based on a simple set point model.

These considerations suggest, therefore, that were animals' body weights controlled by a system similar to that of Fig 1, Keesey's results, as well as those of Hoebel and Teitelbaum [8] and many others, could be accounted for without recourse to the notion of a set point. In other words changes in the set point of a system cannot be inferred from changes in its settling point, nor can the existence of an internal set point be inferred from the fact that a system appears to have a settling point which it will defend. It should be pointed out that if the functions we have symbolized by G were performed in the LH, and those symbolized by H in the VMH, we would have a model for the control of feeding very similar to that of Panksepp [22], except for the additional presence of a set point in his model.

This model suggests that the defense of body weight by animals may reflect not the existence of an internal standard, but rather a constant magnitude of stimuli which drive the intake mechanism. Were this so, one would expect that changes in dietary palatability should greatly effect body weight This has often been shown to be the case (e g., [5,14]), and in fact the fattest rat on record to our knowledge, 1,445 g, was produced not by hypothalamic lesion, but by maintenance on an extremely palatable high fat diet [16]

If body weight is regulated by an internal set point mechanism one naturally wonders why it is singularly ineffective in maintaining a constant weight in the face of altered dietary palatability. Rejection of a set point concept of weight regulation would have the additional advantage of resolving the problem of an animal's willingness to ingest highly palatable substances in the absence of deprivation [10, 23, 16] The importance of external stimulation in controlling feeding behavior is further emphasized by the inability of rats to maintain food intake and consequently body weight in the absence of oropharyngeal stimulation [9].

It has been argued that because individuals of the same species defend different weights, there must exist individual differences in set points [20]. It should be obvious, however, that such differences between individuals, as well as between sexes and age groups, could as well reflect disparate gains (G and H of our model) somewhere within the weight control system In like manner, the changes in body weight associated with hibernation [11], migration [21], and pregnancy [32], could be produced by alterations of gains or by the presence of biasing signals which might, for example, add to S and GW at the summing point shown in Fig 1 In all of these cases, given our current knowledge, it seems to be unnecessary and unparsimonious to introduce the notion of a set point to explain data which can as well be accounted for without its introduction

Although the model which we have proposed here is much too simple to provide an explanation of the control of body weight, it may serve to draw attention to several points. First, it suggests a way in which the effects of variations in the sensory properties of food might be incorporated into a model of body weight control Since it is widely recognized that input from gustatory, olfactory and other sensory systems play a central role in the control of ingestion, and hence body weight, it seems essential that such an input should be an important element of any weight control model. Using sensory stimulation rather than a set point as the input to the system takes account of this point It also emphasizes the fact that the amount of food which an animal ingests may be more dependent on sensory factors than upon an internal drive which arises when nutritional reserves fall below some reference point Secondly, it demonstrates that the postulation of a neural set point is not necessary to account for weight control The fact that a given quantity is, under some circumstances, maintained at a relatively constant value does not by itself imply the existence of an internal reference value This point is relevant not only to the issue of the control of body weight but to any biological control system. For example, regulation and defense of body temperature, or body water does not necessarily imply the existence of set points controlling these variables

In summary, this model suggests a new way of looking at the problem of the control body weight. Alternative ways of looking at problems sometimes lead to progress in a field

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