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Body Weight Setpoint, Metabolic Adaption and Human Starvation

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A biological setpoint for fatness has been proposed in the medical literature. This body weight setpoint functions as a point of stable equilibrium. In an underfed state, with resulting weight loss, the body will reduce the relative energy expenditure by metabolic adaption which reduces the rate of weight loss. Previous mathematical models of energy expenditure and weight loss dynamics have not addressed this setpoint mechanism. The setpoint model has been proposed to quantify this biological process and is unique in predicting energy expenditure during weight loss as a function of the setpoint fat-free mass ratio and setpoint energy expenditure, eliminating the various controlling characteristics such as age, gender and heredity. The model is applied to the seminal Minnesota human semistarvation experiment and is used to predict weight vs time on an individual basis and the caloric requirements for weight maintenance at the reduced weight. Comparison is made with the Harris–Benedict equations and the Brody–Kleiber ($W^{\frac{3}{4}}$) law.

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1. INTRODUCTION

Models of human energy expenditure have been based on equilibrium conditions. These models frequently overestimate the energy needs when applied to weight loss subjects. Medical researchers have proposed that deviation from a genotypically preferred equilibrium or setpoint weight results in metabolic adaption, reducing the relative energy requirements. A model that accurately estimates the caloric needs of a reduced weight individual would be useful in calculating the calories needed to maintain a rate of weight loss or stay at a reduced weight.

We develop a mathematical model for calculating daily energy requirements that includes the metabolic response to weight loss. The proposed metabolic adaption will be based on the setpoint levels of energy, weight and percentage body fat. The model is compared with models based on the Harris–Benedict equations and the Brody–Kleiber ($W^{\frac{3}{4}}$) law in predicting weight loss vs time and the energy requirements of the subjects in the Minnesota human semistarvation experiment. Table 1 provides definitions for abbreviations used.

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Table 1. Definition of terms.

Term	Definition
24EE	24 hour energy expenditure. 24EE = PA + REE (Calories per day)
BK	Brody–Kleiber
C	Daily calorie intake from diet. (Calories per day)
C_0	Equilibrium (setpoint) value of C.
E	Same as 24EE.
E_0	Equilibrium (setpoint) value of E.
FFM	fat-free (body) mass (kg)
FFMR	fat-free (body) mass ratio: FFM/W
FM	(Body) fat mass (kg)
HBE	Harris–Benedict equation
PA	Daily calorie expenditure due to physical activity outside sedentary requirements. (Calories per day)
REE	Resting energy expenditure: daily energy expenditure of a sedentary individual. (Calories per day)
W	Total body weight (mass) W = FM + FFM
W_0	Equilibrium (setpoint) value of W.

2. DISCUSSION

The rate of weight lost during a reduced calorie diet is dependent on an imbalance between the energy provided by the daily calorie intake (C) and the total 24 hour energy expenditure (24EE). Calculating C is merely a matter of calorie counting, while some difficulty arises in estimating 24EE.

Numerous methods exist to predict 24EE and its components: resting energy expenditure (REE) and physical activity (PA). These rates have been correlated to total body weight (W), fat mass (FM) and fat-free mass (FFM). In the Brody–Kleiber law, REE is proportional to W^b (Kleiber, 1975). Through linear regression in the log–log scale the value $b = \frac{3}{4}$ has been determined the best fit for mammals for several orders of magnitude of body weight from mice to elephants. In the classic Harris–Benedict equations (HBE) (Harris and Benedict, 1919), along with updated versions (Mifflin *et al.*, 1990), REE is correlated by multilinear regression to W, gender, age and height. FFM has been reported as a predictor of both 24EE and REE (Cunningham, 1991). Energy expenditure during physical activity has been found to be directly proportional to W (Van der Walt and Wyndham, 1973).

While these methods for estimating energy expenditures may be accurate for long-term equilibrium conditions, they may be inadequate during weight loss conditions. Finer *et al*. (1986) and Foster *et al*. (1995) indicate decreases in 24EE, REE or PA that could not be explained by changes in the controlling body parameters. Leibel *et al*. (1995) reported a decrease in both resting and nonresting energy per kilogram of fat-free mass in both obese and never obese individuals following a 10% weight loss. Weigle (1988) found a reduction in the energy cost of physical activity following a 22% weight loss even with weighted vests compensating for the lost weight.

Medical researchers explain these reduced energy expenditures after weight loss as metabolic adaption, as the body attempts to maintain a genotypical 'normal' weight or setpoint weight (Leibel, 1990; Garner, 1997). In a review article on this subject, Luke and Schoeller (1992) report that the metabolic adaption is noted in both lean and, to a lesser extent, obese weight losers. They also observed that the magnitude of energy reduction correlates most with weight loss and fat-free mass.

The standard models of predicting energy expenditure are inaccurate for weight loss conditions because setpoint driven metabolic adaption is not included. A new method is needed. We propose here a mathematical model that calculates energy expenditure following weight loss from setpoint. The model will be applied to the Minnesota experiment (Keys, 1950) and compared with reference models in the prediction of weight loss dynamics and reduced weight equilibrium.

3. ESTIMATING 24 HOUR ENERGY EXPENDITURE USING THE SETPOINT MODEL

We formulate a model for calculating 24EE following weight loss from setpoint weight based on the following criteria suggested by the introductory discussion:

- Weight loss from setpoint will produce a metabolic adaption that is greater in lean subjects than in the obese.
- The level of adaption will depended on weight.
- The rate of adaption will depend on the setpoint fat-free mass ratio (FFMR) $=$ fat free weight $\div$ total body weight.

We start with the simplest 24EE model where the daily energy expenditure (*E*) is proportional to body weight (*W*). To allow for the metabolic adaption to weight loss, we let the proportionality parameter vary with *W*.

$$E = \alpha(W)W. \tag{1}$$

The coefficient $\alpha(W)$ is a function of weight and is uniquely determined for each individual based on setpoint values. $\alpha(W)$ is expected to decrease as weight falls below setpoint. Equation (1) is only applied to cases of weight change around setpoint and not to calculate the setpoint energy. We model that $\alpha(W)$ changes linearly with W, from the setpoint levels (α_0, W_0) to starvation levels (α_s, W_s). This yields

$$\alpha = \left(\frac{\alpha_s W_0 - \alpha_0 W_s}{W_0 - W_s}\right) + \left(\frac{\alpha_0 - \alpha_s}{W_0 - W_s}\right)W = \alpha_0\left[\left\{\frac{\frac{\alpha_s}{\alpha_0} - \frac{W_s}{W_0}}{1 - \frac{W_s}{W_0}}\right\} + \left\{\frac{1 - \frac{\alpha_s}{\alpha_0}}{1 - \frac{W_s}{W_0}}\right\}\frac{W}{W_0}\right]. \tag{2}$$

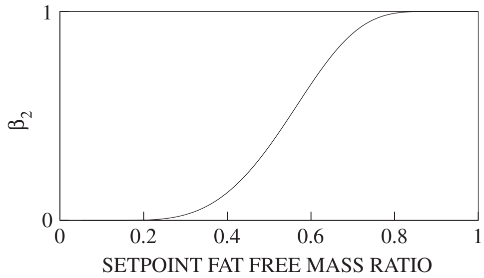

Figure 1. β_2 value vs setpoint fat-free mass ratio from equation (5) ($f = 1.5$ and $m = 0.5$).

Defining

$$\beta_1 = \frac{\frac{\alpha_s}{\alpha_0} - \frac{W_s}{W_0}}{1 - \frac{W_s}{W_0}}; \qquad \beta_2 = \frac{1 - \frac{\alpha_s}{\alpha_0}}{1 - \frac{W_s}{W_0}} \qquad \Rightarrow \qquad \alpha = \alpha_0\left[\beta_1 + \beta_2\frac{W}{W_0}\right]. \quad (3)$$

At the setpoint $E_0 = \alpha_0 W_0$ then equations (1) and (3) yield the setpoint model energy

$$E = E_0\left[\beta_1 + \beta_2\frac{W}{W_0}\right]\frac{W}{W_0}. \quad (4)$$

It is useful to note that all the personal characteristics that affect normal metabolic functions are represented by E_0 and W_0. This makes the model less susceptible to individual variations. However, we must now devise an analysis to predict an individual's β_1 and β_2. Noting that $\beta_1 + \beta_2 = 1$, we require only values of β_2. Given that $\frac{W_s}{W_0} < 1$ and $\frac{\alpha_s}{\alpha_0} < 1$ shows that $\beta_2 > 0$. We assume $\frac{\alpha_s}{\alpha_0} > \frac{W_s}{W_0}$; that the relative per-pound energy requirements will not decrease as fast as the relative weight. So $\beta_1 > 0$. The above implies $0 < \beta_1, \beta_2 < 1$. The rate of metabolic adaption is $\frac{d\alpha}{dW} = \beta_2\frac{\alpha_0}{W_0}$, then $\beta_2 = 0$ yields no adaption while $\beta_2 = 1$ yields the maximum adaption. Following our design criteria: FFMR $= 1 \Rightarrow \beta_2 = 1$ and FFMR $= 0 \Rightarrow \beta_2 = 0$. Allowing for the fact that FFMR $= 0$ or 1 is not physically possible, the values of β_2 = 0 and 1 should be nearly reached for more reasonable values of FFMR. A function that meets these requirements is

$$\beta_2 = \frac{\tanh\left[\frac{f(\text{FFMR}-m)}{\text{FFMR}*(1-\text{FFMR})}\right] + 1}{2}. \quad (5)$$

The value of m determines the inflection point and the value of f determines the maximum slope at the inflection point. Figure 1 depicts the graph of β_2 vs FFMR.

4. Models for Comparison

We establish two models, based on the Harris–Benedict equations and the Brody–Kleiber law, for comparison with the setpoint model.

4.1. ***The Harris–Benedict equations.*** Using a Harris–Benedict (Harris and Benedict, 1919) form equation to determine resting energy

$$\mathrm{REE} = \alpha_{r0} + \alpha_{r1} W. \tag{6}$$

Note that α_{r0} is dependent on the individual's height, age, and gender. Both α_{r0} and α_{r1} will be constant for any weight loss regime. Using $\mathrm{PA} = \alpha_p W$ (Van der Walt and Wyndham, 1973), the total energy expenditure is

$$E = \mathrm{PA} + \mathrm{REE} = \alpha_{r0} + (\alpha_{r1} + \alpha_p) W = \alpha_{c_0} + \alpha_{c_1} W. \tag{7}$$

Since

$$\frac{dE}{dW} = \alpha_{c_1} \Rightarrow \text{ constant slope} \tag{8}$$

this model shows no change in the rate of energy expenditure per pound, that is no metabolic reduction.

4.2. ***The Brody–Kleiber model.*** The Brody–Kleiber equation is (Kleiber, 1975):

$$\mathrm{REE} = \alpha_{bk} W^{\frac{3}{4}}. \tag{9}$$

Adding a term for physical activity:

$$E = \alpha_p W + \alpha_{bk} W^{\frac{3}{4}}. \tag{10}$$

4.3. ***Comparison models.*** The setpoint model is constructed such that $E = E_0$ when $W = W_0$. A valid comparison of the models requires a similar treatment for the Harris–Benedict (constant slope) and the Brody–Kleiber models. Analysis reveals that the form $E = E_0\left(\frac{W}{W_0}\right)$ yields a lower boundary on any constant slope form passing through (E_0, W_0). Similarly the Brody–Kleiber total is bounded above by $E = E_0\left(\frac{W}{W_0}\right)^{\frac{3}{4}}$ and below by the constant form. Therefore the following two models will be used:

The constant (Slope) model.

$$E = E_0\left(\frac{W}{W_0}\right). \tag{11}$$

The $\frac{3}{4}$ power model.

$$E = E_0\left(\frac{W}{W_0}\right)^{\frac{3}{4}}. \tag{12}$$

Figure 2, showing the relative weight vs energy for the above models, should be read from right to left. As the relative weight decreases the relative energy requirement decreases more slowly for the $\frac{3}{4}$ power model (dotted) than for the constant model (dashed) but more quickly for the setpoint model (solid) with β_2 values of 0.2, 0.4, 0.6, 0.8 and 1.0 (left to right). The actual HBE and Brody–Kleiber results would lie between the dashed and dotted lines.

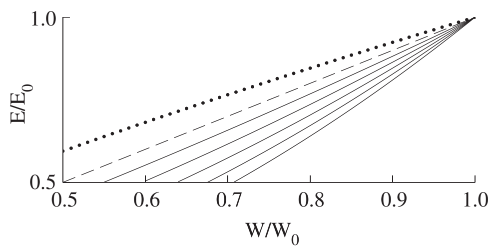

Figure 2. Setpoint relative 24 hour energy expenditure vs weight for the $\frac{3}{4}$ power law (dotted), the constant model (dashed) and the setpoint model (solid, $\beta_2 = 0.2$, 0.4, 0.6, 0.8 and 1.0 from left to right). Note $\beta_2 = 0$ corresponds to the constant model.

4.4. ***Setpoint metabolic adaption.*** Substituting $\beta_1 = 1 - \beta_2$, equation (4) can be written as

$$E_{sp} = E_0\left(\frac{W}{W_0}\right) - \beta_2\left[\frac{W}{W_0} - \left(\frac{W}{W_0}\right)^2\right]E_0. \tag{13}$$

The setpoint model energy is equivalent to the constant model with a metabolic adaption (reduction) represented by the term $\beta_2\left[\frac{W}{W_0} - \left(\frac{W}{W_0}\right)^2\right]E_0$.

5. The Minnesota Experiment

A test of the setpoint model requires a diet-induced weight loss from setpoint, with knowledge of the setpoint weight, 24EE and FFMR, as well as the calories provided by the diet regime. The physical activity during the dieting phase must remain constant and equal to that displayed during the setpoint maintenance or any changes must be quantified. Additionally, the physical activity must be associated with moving one's own body weight (e.g., climbing stairs and walking) which is expected to decrease with loss of body weight and not lifting activities such as loading or unloading a truck. These somewhat strict requirements are exactly provided by the seminal human starvation study referred to as the Minnesota experiment.

The Minnesota experiment was conducted during the last months of World War II using 32 volunteer conscientious objectors. The subjects were monitored during a three month control period establishing an equilibrium body weight and calorie consumption for a specified activity regime. A 6 month dieting period followed with the goal of 25% weight loss. The daily average calories were adjusted weekly to provide weight vs time along a parabolic path flattening near the end of the period. The dieting period was followed by a 3 month rehabilitation period during which calorie consumption was gradually increased. An extensive report of the data taken during these periods is provided in Keys (1950). Figure 3(a) shows the weekly averages of the daily calories consumption relative to the setpoint for the 32 individuals of the Minnesota experiment. The severity of the diet is clear with an average drop in calories of more than 50% during the 24 weeks of weight loss.

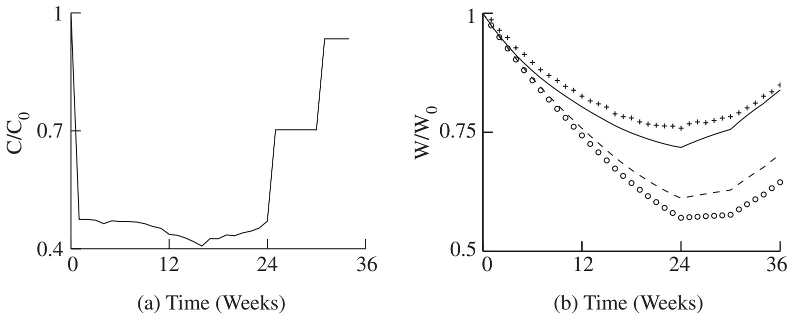

Figure 3. (a) Average weekly calories relative to the setpoint calories for 32 individuals of the Minnesota experiment and; (b) averages of $\left(\frac{W}{W_0}\right)$ for 32 individuals of the Minnesota experiment: data (+++), the setpoint model (——), constant model (- - -) and $\frac{3}{4}$ power law (ooo).

Calories are increased during the rehabilitation period (weeks 25–36). Figure 3(b) shows the weekly average of the body weights relative to the setpoint. The data (+++) shows the parabolic weight loss curve and weight increase during rehabilitation.

6. APPLICATION

We apply the law of conservation of energy to the human body: the rate of change of the energy stores is equal to the rate of energy supplied less the rate of energy expended. The change in body weight is converted to energy by the factor k. In equation form

$$k\frac{dW}{dt} = C - E, \qquad W(0) = W_0. \tag{14}$$

The dimensions of the parameters are as follows: $|W| =$ kilogram; $|t| =$ days and $|E| = |C| =$ Calories per day. We use $k = 7770$ Calories per kilogram to convert body mass to energy. The values of E are provided for each model as outlined above with all necessary data taken from Keys' report. Since the C values changed on a weekly basis [see Fig. 3(a)], equation (14) must be solved numerically [See Kozusko (1999) for analysis of analytic solutions].

Setting $\frac{dW}{dt} = 0$ in equation (14) yields $C = E$, then model equations (4), (11) and (12) provide the daily calorie requirement for weight maintenance at a weight below the setpoint. If the physical activity is changed from the setpoint levels, these changes can be applied to the model equations. Adjusting the setpoint energy equation (4) for change in energy requirements:

$$E = E_0\left[\beta_1 + \beta_2\frac{W}{W_0}\right]\frac{W}{W_0} - \Delta E \quad \Rightarrow \quad \frac{E}{E_0} = \left[\beta_1 + \beta_2\frac{W}{W_0}\right]\frac{W}{W_0} - \frac{\Delta E}{E_0} \tag{15}$$

Table 2. Root mean square values of the setpoint relative weights $\left(\frac{W}{W_0}\right)$ of models vs data for the 36 weeks starvation and rehabilitation periods of the individual subjects of the Minnesota experiment.

Subject	Setpoint model	Constant model	Power law model	Subject	Setpoint model	Constant model	Power law model
1	0.0200	0.0664	0.0977	101	0.0414	0.1241	0.1590
2	0.0245	0.0650	0.0919	102	0.0194	0.0986	0.1307
4	0.0089	0.0829	0.1163	104	0.0142	0.0931	0.1258
5	0.0400	0.0301	0.0564	105	0.0108	0.0755	0.1058
8	0.0458	0.1317	0.1683	108	0.0740	0.1559	0.1894
9	0.0633	0.1571	0.1949	109	0.0242	0.0644	0.0930
11	0.0183	0.0596	0.0894	111	0.0407	0.1328	0.1707
12	0.0307	0.1038	0.1352	112	0.0725	0.1698	0.2099
19	0.0150	0.0797	0.1121	119	0.0087	0.0760	0.1080
20	0.0246	0.1135	0.1504	120	0.0192	0.0613	0.0923
22	0.0253	0.1104	0.1451	122	0.0237	0.0609	0.0937
23	0.0242	0.0596	0.0918	123	0.0807	0.1758	0.2144
26	0.0347	0.1172	0.1499	126	0.0289	0.1019	0.1306
27	0.0145	0.0737	0.1052	127	0.0426	0.1438	0.1850
29	0.0210	0.0895	0.1232	129	0.1101	0.2228	0.2690
30	0.0659	0.1596	0.1970	130	0.0804	0.1726	0.2105

Table 3. Root mean square values of models vs data.

	Setpoint model	Constant model	Power law model
Average of RMS	0.0365	0.1072	0.1410
RMS of Averages	0.0277	0.1063	0.1403

and for the constant and $\frac{3}{4}$ power models respectively:

$$\frac{E}{E_0} = \frac{W}{W_0} - \frac{\Delta E}{E_0}, \qquad \frac{E}{E_0} = \left(\frac{W}{W_0}\right)^{\frac{3}{4}} - \frac{\Delta E}{E_0}. \tag{16}$$

7. RESULTS

Results are presented graphically in Figs 3(b) and 4, and Tables 2–4. Figure 3(b) displays the weekly data averages of the setpoint normalized weights of the 32 individuals of the Minnesota experiment and the averages of the normalized numerical solutions of equation (14) using the energy model equations (4), (11) and (12). Because the setpoint model is based on the individual's setpoint parameters and attempts to model the individual's response to weight loss, the data and the solutions for each individual are presented in Fig. 4.

Table 4. Average setpoint relative calorie ratio for weight maintenance at 75% setpoint weight, corrected for an 11% reduction in energy requirement from reduced physical activity.

	Data	Setpoint model	Constant model	Power law model
Calorie Ratio	0.4500	0.4525	0.6400	0.6959

To provide a quantitative evaluation of the model results, the root mean square (RMS) of the differences between model predictions and the data of the setpoint relative weights for the 36 weeks period are displayed in Table 2. In all but one case (Subject 5), the setpoint method has a substantially lower RMS value. The averages of the RMS values of Table 2 and the RMS of the averages displayed in Fig. 3(b) are presented in Table 3. The average RMS values indicate that the setpoint model is closer to modeling the data by the equivalent of 7–10% of the setpoint weight when compared to the other two models.

Taylor and Keys (1950) reported that the subjects in the Minnesota experiment were able to maintain an energy balance with 45% of the calories at 75% body weight when compared to the prestarvation values but also indicate an 11% average energy reduction due to a cutback in physical activities. The participants in the Minnesota experiment were young men with low body fat, so $\beta_2 \approx 1.0$. Substituting $\beta_2 = 1.0$ ($\beta_1 = 0$), $\frac{W}{W_0} = 0.75$ and $\frac{\Delta E}{E_0} = 0.11$ into equations (15) and (16) yields the results in Table 4. The comparison models greatly overestimate the actual energy requirements at the reduced weight.

8. Summary and Conclusions

The setpoint model provides a unique method for calculating an individual's 24EE during diet-induced weight loss conditions by incorporating the body's energy conservation as the body attempts to limit the loss of weight from it's biologically desired setpoint weight. It is significant in modeling the individual specifically based on the individual's setpoint values, eliminating the need to fit the individual to a universal model based on various body parameters such as age, gender, height and weight. Using the setpoint model in equation (14) will yield a better prediction of weight loss than those provided by equilibrium-based energy expenditure models. The setpoint model is flexible enough to allow for variation in energy requirements due to changes in physical activity and can be used to calculate the energy (Calories) required for weight maintenance at a reduced weight. The setpoint model's more accurate prediction of a weight loss regime will be beneficial to dieters, who might lose will-power if the actual rate of weight loss is less than predicted.

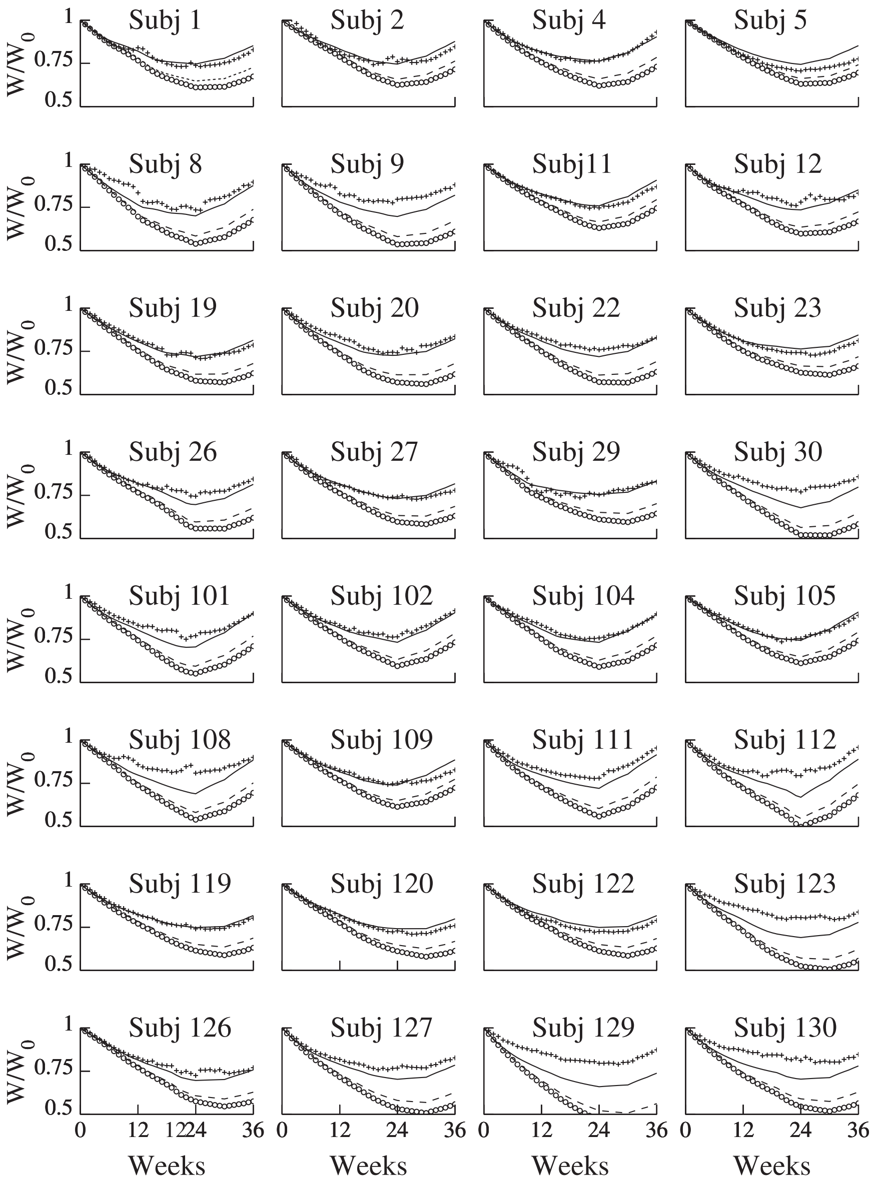

Figure 4. Setpoint relative weight $\left(\frac{W}{W_0}\right)$ for individuals of the Minnesota experiment: data (+++), the setpoint model (——), constant model (- - -) and $\frac{3}{4}$ power law (ooo).

The application of the setpoint model to The Minnesota experiment tests the model at it's most active limits, with a 25% weight loss forced on individuals with low body fat and thus an expected high metabolic adaption ($\beta_2 \approx 1.0$). However, the model predicts some feedback for most individuals and so some differences in outcomes of reduced-calorie diets when compared to the equilibrium models. More research is necessary to refine the shape of Fig. 1 and to study weight loss regimes for individuals with ranges of body fat and thus ranges of β_2.

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