"Set-point," "starvation response," and "metabolic adaptation" theories are not supported by the literature

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It's not uncommon to hear both lay persons and professionals matter-of-factly refer to the "starvation response" (also called metabolic adaptation) and "set-point theory" as if they were accepted facts. The supposition of these theories is that the body reacts to reduced energy intake, or weight loss, by lowering its basal metabolic rate in an attempt to maintain the current weight or return to a higher weight. If this were the case the data would show a suppressed resting metabolic rate (RMR) per kilogram of fat free mass (FFM) after weight loss.

These theories however, have not survived sound scientific investigation, and those researchers who are familiar with this area of medical literature have known that for almost 20-years. Three comprehensive reviews of the literature in 1992, 1994, and 1995[1,2,3] all reached the same conclusions that:

- Dieting does not lead to an abnormal decrease in basal metabolic rate. *A lower body weight does mean a lower BMR, however it is not abnormal to the new reduced weight level.*
- Dieting does not lead to an abnormal loss of lean body mass, or redistribution of body fat. *When people gain weight part of their weight gain is lean body mass (muscle). When they lose weight they tend to lose the same ratio of fat and muscle that they originally gained*.[4]
- Dieting does not affect the future ease/difficulty of regaining/losing weight (at least from a physiological basis).

While those three reviews looked at the literature regarding people who were *trying to lose weight*, other research has looked at *chronically undernourished* populations expecting to find proof of metabolic adaptation, but the data simply do not support the theory.[5,6,7]

Shetty's paper[5] was a review of existing literature regarding "metabolic adaptation," or set-point theory, which he presented as the keynote lecture at a scientific meeting of the Nutrition Society in July 1992. Shetty reported that many studies on malnourished subjects, have failed to demonstrate any significant decrease in metabolic rate when adjusted per kg/FFM. In fact, most recent measurements show an increased RMR kg/FFM in undernourished individuals. Finding a higher RMR kg/FFM makes sense due to changes within the *lean body mass* compartment, which result in a higher proportion of organ tissue (and less skeletal muscle), and therefore a higher RMR per Kg/FFM. The author summarizes, "*It would then appear that an increase in metabolic efficiency in the RMR component of the energy expenditure, which has been hitherto considered to be the cornerstone of the beneficial metabolic adaptation to energy inadequacy, is of doubtful existence*." The author goes on to discuss the literature, and finally concludes that the data do not demonstrate adaptive responses in RMR, thermogenesis, or physical activity, in chronically undernourished subjects.

One of the early problems with this area of literature was with the statistical analysis of the follow-up measurement of RMR per Kg/FFM. Researchers must adjust for changes in fat mass and LBM correctly to determine if any differences between the baseline and follow-up RMR remain. Some older studies (that seemed to support the notion of metabolic adaptation)[8,9] used a ratio method to normalize the follow-up RMR for changes in FFM, which led to the follow-up RMR *appearing falsely lower* than it actually was. Well done studies use analysis of covariance (ANCOVA), which is the appropriate method for the *curvilinear* relationship between RMR and FFM. The ratio method should only be used when adjusting factors that have a *linear* relationship, which is not the case between fat and FFM.

Note that the paper by Leibel,[9] which may be the most quoted among advocates of the set-point idea is one of the studies criticized for the above statistical error, "*Leibel et al, reported that weight loss caused a reduced ratio of RMR to FFM; however, when the authors adjusted RMR for changes in FFM and FM by using a regression-based analysis [ANCOVA], the changes in RMR were not significant...*"[10].

Weinsier, regarding his 4-year study comparing post-obese women to controls, concluded that exogenous factors contributed to weight regain, rather than any inherent set-point. Over the four years, some women regained as little as 2 kg and others as much as 26 kg. *"Overall our data suggest that this tendency to weight regain among obesity prone women is more likely to*

be due to maladaptive responses to the environment in terms of physical inactivity or excess energy intake than to reduced energy requirements."[11]

It's important to note that while dieting does not lead to a *permanent* suppression in RMR there can be *temporary* suppression *while following* reduced energy intakes. Since this suppression disappears following cessation of negative energy balance it is not evidence for (the original versions of) set-point or starvation-response theories.

Additionally, the majority of dieters will see little or no suppression anyway. Poehlman explains "*the data are completely equivocal—RMR doesn't always drop with energy restriction… the trend [however] is that the greater the [magnitude of] energy restriction the greater the potential reduction in adjusted RMR.*"[12] Another review on this topic concludes that for subjects on low-calorie diets (LCDs) of ≥1,200 calories the reduction in adjusted RMR (if any) is modest at 0% to 5%. Conversely, a 5% to 15% reduction can be seen with very low calorie diets (VLCDs), which by definition are ≤800 calories.[13] It should be noted that many subjects enrolled in VLCD programs consume 1,200 to 1,600 kcals per day, or more.

These data should be viewed as good news for a couple of reasons. First, most people are consuming ≥1,200 calories/day, and for many of them we can expect modest effects, if any, on their RMR. Remember, however, that the magnitude of energy restriction is the key factor.

Secondly, for those people who are on VLCDs, even a 15% drop in RMR isn't a justification for *significantly* stalled weight loss. For example, the rate of weight loss for a 300-pound female (based on predicted RMR) would be 80% of what it would have been before the depression in RMR—meaning that she would still have significant weekly weight loss assuming compliance with assigned calorie intake.

De Groot investigated whether a slimming diet that *alternated low* and *normal* energy intake (a rotation diet) would counteract a decrease in 24-hour energy expenditure (EE) compared to subjects following a low calorie diet (it did not). De Groot concluded, *"because the decrease in 24EE could be explained by changes of body weight, energy intake (thermic effect of food) and physical activity, there was no need to theorize about the influence of other adaptive mechanisms.*"[14]

De Groot's findings are not surprising since it takes 7- to 14-days on *maintenance level calories* (appropriate for current body weight) for a subject's RMR to normalize following energy restriction.[15]

Taking the follow-up RMR measurement *before* patients were stabilized is another example of how some studies have provided misleading follow-up RMRs kg/FFM. If a study doesn't specify when the reading was taken it makes it difficult to conclude anything from the data without contacting the study authors for clarification.

When it does occur, the suppression in RMR secondary to *ongoing negative energy balance* is believed to be due to several factors the greatest probably being the suppression of both active thyroid hormone (T_3) and sympathetic nervous system (SNS), in addition to changes in insulin, glucagon, growth hormone and glucocorticoids. Weinsier suggested that normalized T_3 could be used as an indicator of weight stabilization that researchers could look for *before* attempting to measure the post weight loss RMR.

Untreated hypothyroidism can lower REE 30% ±10%, while subclinical hypothyroidism is estimated to lower REE 15% ±5%.[16,17,18] Approximately 10% and 7.5% of the population has either frank or subclinical hypothyroidism respectively, with around 80% of cases being in females. Some data indicate that about 40% of treated hypothyroid cases may not be properly adjusted, and may still exhibit various symptoms of hypothyroidism (low body temperature, dry skin, hair loss, depression, low REE, etc.).[19]

Evaluating thyroid status, as well as RMR, before energy restriction commences would provide valuable information for all involved.

The *set-point, starvation-response,* and lately the popular *metabolic-adaptation* theories have evolved over the years as their advocates attempt to maintain a viable theory. Are there physiological changes associated with energy restriction? Yes. Do they prevent weight loss, or maintenance of weight loss? No. The danger with these theories is how they are applied by the public and some professionals. If you *believe* you have no control over your weight that will become a *self-fulfilling prophesy*. One could argue that these notions have done as much to promote the obesity epidemic as the cultural and environmental changes that clearly encourage it.

[1] Wing R, et al. *Weight cycling in humans: a review of the literature.* Ann Behav Med 1992;14:113-119.

[2] NIH National Task Force on the Prevention and Treatment of Obesity. *Weight Cycling.* JAMA Oct. 19, 1994;272(15):1196-1202. This study was conducted by an expert panel at the National Institutes of Health, which consisted on experts in the fields of nutrition, obesity, and epidemiology.

[3] Muls E, et al. *Is weight cycling detrimental to health? A review of the literature in humans*. Intl J Obes 1995;19(3):46S-50S.

[4] Wadden TA, et al. *Effects of weight cycling on the resting energy expenditure and body composition of obese women.* Int J Eat Disord 1996 Jan;19(1):5-12.

[5] Ferro-Luzzi A, et al. *Basal metabolism of weight-stable chronically undernourished men and women: lack of metabolic adaptation and ethnic differences.* Am J Clin Nutr 1997;66:1086-93. This author is a pioneer of metabolic adaptation/set-point theory, so her conclusions here represent an "about face" forced by her ongoing collection of data, and the fields' understanding of how to correctly make comparisons in RMR between subjects, or in handling pre and post obese subjects.

The author notes that normalizing BMR, for either body weight or FFM, by analysis of covariance abolished all difference in BMR between well-nourished and chronically-undernourished subjects. The author concludes: "These findings suggest the absence of an enhanced metabolic response in weight-stable chronically undernourished adults. This is in contrast with earlier reports, and supports more recent views."

In further discussion the author notes that her data, and that of previous reports (Gambian men and women, Ethiopian women, and malnourished Colombian school-aged boys and girls), found a higher BMR per unit of body weight or FFM, compared to well-nourished controls. This finding is consistent with the loss of tissues that are less metabolically active (adipose tissue, and skeletal muscle), vs. highly metabolically active tissues (organs).

[6] Shetty PS. *Chronic undernutrition and metabolic adaptation*. Proceedings of the Nutrition Society. 1993;52:267-284.

[7] **Soares** MJ, et al. *Basal metabolic rates and metabolic efficiency in chronic undernourished.* Euro J Clin Nutr. 1991;45:363-373. "A large number of measurements made, over the last decade, in chronically energy deficient (CED) subjects do not confirm the existence of an enhanced metabolic efficiency as indicated by a reduce O_2 consumption per unit FFM. On the contrary, it has now been observed that the BMR expressed per kg/FFM was significantly higher in CED subjects than in well-nourished subjects."

[8] Weigle DS, et al. *Weight loss leads to a marked decrease in nonresting energy expenditure in ambulatory human subjects.* Metabolism. 1998;37;(10):930-836.

[9] Leibel RL, et al. *Changes in energy expenditure resulting from altered body weight*. N Engl J Med 1995;332:621-8.

[10] Weinsier RL, et al. *Energy expenditure and free-living physical activity in black and white women: comparison before and after weight loss.* AJCN 2000;72:1088-94.

[11] Weinsier RL, et al. *Metabolic predictors of obesity*. J Clin Invest 1995;95:980-985.. There was no significant difference in REE between the obese and post-obese states after adjusting for FFM and FM. The average value for TEF was lower in the obese subjects compared to controls ($P < 0.05$); however, it rose after weight loss such that there was no longer a significant difference in TEF between the post-obese and never-obese controls.

[12] Poehlman ET, Melby CL, Goran MI. *The Impact of Exercise and Diet Restriction on Daily Energy Expenditure*. Sports Med. 1991;11:78-101.

[13] Prentice A, Goldberg GR, Jebb SA, et al. *Physiological Responses to Slimming*. Proc Nutr Soc. 1991;50:441-458.

[14] de Groot LC, et al. *Adaptation of energy metabolism of overweight women to altering and continuous low-energy intake.* Am J Clin Nutr 1989;50(6):1314-23.

[15] Weinsier RL, et al. *Do adaptive Changes in Metabolic Rate Favor Weight Regain in Weight Reduced Individuals?* Am J Clin Nutr. 2000;72:1088-1094.

[16] DuBois EF. *Basal Metabolism in Health and Disease.* 3rd ed. Philadelphia, PA: Lea and Febinger; 1936.

[17] Freake HC, Oppenheimer JH. *Thermogenesis and thyroid function. Annu* Rev Nutr. 1995;15:263-91.

[18] Staub JJ, Althaus BU, Engler H, Ryff AS: *Spectrum of Subclinical and Overt Hypothyroidism: Effect on Thyrotropin, Prolactin, and Thyroid Reserve, and Metabolic Impact on Peripheral Target Tissues*. Am J Med. 1992;92:631-642.

[19] Canaris GJ, Manowitz NR, Mayor G, Ridgway EC: *The Colorado thyroid disease prevalence study.* Arch Intern Med 2000;160:526-34.