

14. Franz MJ, VanWormer JJ, Crain AL, et al. Weight-loss outcomes: a systematic review and meta-analysis of weight-loss clinical trials with a minimum of 1-year follow-up. *J Am Diet Assoc* 2007;107:1755–1767
15. U.K. Prospective Diabetes Study Group. Response of fasting plasma glucose to diet therapy in newly presenting type II diabetic patients. *Metabolism* 1990;39:905–912
16. Weyer C, Bogardus C, Mott DM, Pratley RE. The natural history of insulin secretory dysfunction and insulin resistance in the pathogenesis of type 2 diabetes. *J Clin Invest* 1999;104:787–794
17. Academy of Nutrition and Dietetics. Diabetes mellitus type 1 and 2 systematic review and guideline, 2015 [Internet]. Available from <http://www.andeal.org/topic.cfm?menu-5305>. Accessed January 2017
18. Franz MJ, MacLeod J, Evert A, et al. Academy of Nutrition and Dietetics nutrition practice guideline for type 1 and type 2 diabetes in adults: systematic review of evidence for medical nutrition therapy effectiveness and recommendations for integration into the nutrition care process. *J Acad Nutr Diet*. In press
19. Cefalu WT, Bray GA, Home PD, et al. Advances in the science, treatment, and prevention of the disease of obesity: reflections from a *Diabetes Care* editors' expert forum. *Diabetes Care* 2015;38:1567–1582
20. American Diabetes Association. Obesity management for the treatment of type 2 diabetes. Sec. 7 in *Standards of Medical Care in Diabetes—2017*. *Diabetes Care* 2017;40(Suppl. 1):S57–S63
21. Schauer PR, Kashyap SR, Wolski K, et al.; STAMPEDE Investigators. Bariatric surgery versus intensive medical therapy in obese patients with diabetes. *N Engl J Med* 2012;366:1567–1576

Why Weight Loss Maintenance Is Difficult

Alison B. Evert¹ and Marion J. Franz²

■ **IN BRIEF** This article reviews studies related to biological mechanisms that make weight loss maintenance difficult. Approximately 50% of weight variance is reported to be determined by genetics and 50% by the environment (energy-dense foods and reduced physical activity). Body weight is tightly regulated by hormonal, metabolic, and neural factors. Hormonal adaptations (decreases in leptin, peptide YY, cholecystokinin, and insulin and increases in ghrelin, glucagon-like peptide 1, gastric inhibitory polypeptide, and pancreatic polypeptide) encourage weight gain after diet-induced weight loss and continue for at least 1 year after initial weight reduction. Weight loss also results in adaptive thermogenesis (decreased resting metabolic rate), which is also maintained long-term. Neural factors such as dopamine also signal the need to respond to an increased desire for fatty foods after weight loss.

Health care providers (HCPs) often find that people trying to “solve” a weight loss maintenance problem feel guilty about their weight issues. They have been told by family, friends, the public, and, yes, even HCPs that it is their fault—that they simply lack willpower—or have decided on their own that it is their fault that they are regaining the weight they have worked so hard to lose. If they would just continue to eat less and exercise more, the problem would be solved. It sounds

so simple! Yet, anyone dealing with weight loss maintenance issues realizes it is not that simple. The cycle of less weight loss than expected or wanted and subsequent weight regain continues, despite individuals' best efforts to prevent it. In fact, we would probably all agree that, if they were so simple to solve, the issues of weight loss and maintenance would not continue to be problems.

It is claimed that “many clinicians are not adequately aware of the reasons that individuals with obesity

¹University of Washington Medical Center—Diabetes Care Center, Seattle, WA

²Nutrition Concepts by Franz, Minneapolis, MN

Corresponding author: Marion J. Franz, marionfranz@aol.com

<https://doi.org/10.2337/ds017-0025>

©2017 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. See <http://creativecommons.org/licenses/by-nc-nd/3.0> for details.

struggle to achieve and maintain weight loss, and this poor awareness precludes the provision of effective intervention” (1). Many HCPs are reported to hold strong negative attitudes and stereotypes about people with obesity. These attitudes may affect the care they provide. Among people with obesity, experiences of or expectations for poor treatment may cause stress and avoidance of care, mistrust of doctors, and poor adherence. A suggested potential strategy to reduce the impact of obesity stigma on quality of care is to educate HCPs (and patients) about the genetic, environmental, biological, psychological, and social contributors to weight gain and loss (2). HCPs who understand the problem are reported to have more positive attitudes toward patients with obesity (3). However, evidence is lacking regarding whether individuals who are overweight or obese and who better understand the known factors contributing to their problem experience an easing of their guilt burden or whether this knowledge makes solving the problem easier.

Reducing caloric intake results in acute compensatory changes, including increases and decreases in hormones that affect appetite, reductions in energy expenditure, and increases in appetite, all of which promote weight regain. In this article, we summarize several biological factors—genetics, the body’s adaptive hormonal changes that occur with weight loss, adaptive thermogenesis that reduces energy needs, and neural issues that affect appetite—all of which make weight loss maintenance difficult. Although both the environment (4) and mitochondrial dysfunction (5) also contribute to obesity, their roles in weight loss maintenance are less well documented and so are not addressed in this article. In addition, as reviewed elsewhere in this From Research to Practice section (p. 149), people with diabetes compared to those without diabetes lose less weight from simi-

lar weight loss interventions (WLIs), although the pattern of weight loss, weight maintenance, and weight regain is similar. At 6 months from similar WLIs, individuals without diabetes lost an average 7.1 kg, whereas people with diabetes lost an average 3.1 kg. Plateaus and gradual weight regain then occurred. At 12 months, individuals without diabetes had lost an average 5.0 kg compared to 2.9 kg in those with diabetes; at 2 years, the respective losses were 4.1 and 2.8 kg. At 4 years, individuals without diabetes lost an average 3.8 kg; no 4-year studies of similar WLIs in people with diabetes were found (6,7). When treatment is discontinued, weight gain occurs; however, with support, studies report that modest weight loss can be maintained (6,7).

Genetics

The prevalence of overweight and obesity is increasing worldwide and coincides with the abundance of energy-dense foods and reduced physical activity (environmental factors), all of which contribute to the increase. However, not all people living in this obesogenic setting become obese, suggesting that the response to influences in our environment is also determined by other factors, such as genetic makeup (8). Results from twin, family, and adoption studies have consistently estimated that 40–70% of variance in BMI is related to heritability, suggesting that about half of the variance in body size can be attributed to genes, with the other half due to environmental influences (8).

Large-scale genome-wide studies have identified nearly 150 genetic variants significantly associated with cross-sectional measures of BMI, waist circumference, or obesity risk in multiple populations (9). The most consistent findings are those for pathways affecting central nervous system processing and neural regulation of feeding, as well as genes associated with fasting insulin secretion and action. However, for many genome

variants, the underlying biology that links the variant to body weight regulation is unclear.

Although a genetic basis for obesity and the response to changes in energy balance has been clearly established, how to use this knowledge in the clinical management of obesity has not been determined (8). The National Institutes of Health working group on using genomic information to guide weight management states that trials specifically designed to assess the combined effects of genotypes and effective interventions are needed to help move obesity prevention and treatment from universal to precision approaches (9).

Hormonal Adaptations to Weight Loss

Body weight is tightly regulated by hormonal, metabolic, and neural factors. Reducing food intake leads to a negative energy balance that triggers a series of central and peripheral compensatory adaptive mechanisms designed to prevent starvation (10). Body weight is centrally regulated, primarily in the hypothalamus, by peripheral hormonal signals released from the gastrointestinal tract, pancreas, and adipose tissue that regulate food intake and energy expenditure (11). Identified modulators of appetite include leptin, ghrelin, cholecystokinin, peptide YY, insulin, pancreatic polypeptide (PP), glucagon-like peptide 1 (GLP-1), and gastric inhibitory polypeptide (GIP). Table 1 summarizes the primary release site of these hormones, their primary modulator action, and changes with reduced energy intake.

Decreases in leptin levels result within 24 hours of energy restriction. It has been suggested that leptin’s primary role is the prevention of starvation, rather than the regulation of weight (10). Regardless of its primary role, reductions in leptin secretion increase appetite, leading to excess food intake, which can lead to weight regain (12). Insulin levels also decrease, slowing fat metabolism,

TABLE 1. Peripheral Hormonal Signals Released as Adaptations to a Reduced Energy Intake and That Regulate Food Intake and Energy Expenditure (10,12–15)

| Primary Site of Hormone Release | Primary Action | ↑ or ↓ With Reduced Energy Intake |
|------------------------------------|------------------------------------|-----------------------------------|
| <i>Gastrointestinal tract</i> | | |
| Ghrelin (stomach) | Stimulates hunger | ↑ |
| GLP-1 (intestinal mucosa) | Reduces food and calorie intake | ↑ |
| GIP (intestinal mucosa) | Promotes energy storage | ↑ |
| Cholecystokinin (small intestine) | Promotes satiety | ↓ |
| Peptide YY (small bowel and colon) | Promotes satiety | ↓ |
| <i>Pancreas</i> | | |
| Insulin | Slows fat metabolism | ↓ |
| PP | Decreases appetite and food intake | ↑ |
| <i>Adipose tissue</i> | | |
| Leptin (white and brown fat cells) | Increases appetite | ↓ |

potentially in an attempt to preserve energy stores (13). In addition to the effects of leptin and insulin, increases in ghrelin stimulate hunger, and decreases in peptide YY and cholecystokinin promote satiety (10). Increases in GLP-1 result in reduction in food and calorie intake (14), whereas increases in PP cause a sustained decrease in both appetite and food intake, and increases in GIP promote energy storage (15).

After weight loss and the high rate of weight regain after WLI were documented, it became important to know whether these changes in circulating levels of hormones involved in the regulation of body weight were transient or persisted over time. An important study determined baseline, 10-week (after a weight loss program began) and 62-week levels of circulating leptin, ghrelin, peptide YY, GIP, GLP-1, amylin, PP, cholecystokinin, and insulin and subjective ratings of appetite (16). One year after initial weight reduction, levels of circulating hormones that encourage weight regain after weight loss had not reverted to levels recorded before the weight loss. The researchers concluded that the high rate of relapse among obese people who have lost weight has a strong physiological basis based on long-term hormonal

changes and is not simply the result of voluntary resumption of old habits.

Adaptive Thermogenesis

Adaptive thermogenesis (also termed metabolic adaptation) is defined as a slowing of resting metabolic rate (RMR), resulting in a decrease in energy expenditure beyond what would have been predicted by measured changes in body composition such as the loss of fat-free mass and fat mass. This metabolic adaptation is likely needed as a biologically meaningful survival mechanism that conserves energy in the face of starvation and dangerously low energy supplies (17). A number of studies have reported significant reductions in energy expenditure during and shortly after weight loss to levels below predictions based on weight loss and body composition changes; these reductions may predispose to weight regain. A meta-analysis performed on a large sample of RMR data in formerly obese and never-obese individuals showed that, after differences in body size and composition were taken into account, formerly obese individuals had 3–5% lower RMR than did never-obese individuals (18).

To determine whether adaptive thermogenesis is continued during weight maintenance after weight loss, a 1-year study was conducted in

individuals who followed a very-low-energy diet for 8 weeks, followed by a 44-week period of weight maintenance (19). Measurement of energy expenditure and body composition showed that a disproportional adaptive thermogenesis developed during weight loss and was continued for the 44-week period. Individuals with a larger weight loss showed a greater reduction in RMR and, if weight maintenance was unsuccessful, with a return to or beyond baseline weight, adaptive thermogenesis was no longer observed. The researchers concluded that adaptive thermogenesis during weight maintenance increases the risk of weight regain.

It had been suggested that, for successful weight losers, the adaptive thermogenesis persists for many years after weight loss. To determine the accuracy of this assumption, long-term changes in RMR and body composition after weight loss were measured in 14 of the 16 original participants in “The Biggest Loser” competition (20). Measurements were made at baseline, at the end of the 30-week competition, and 6 years later. Despite substantial weight regain, RMR remained as it was at the end of the competition: ~500 kcal/day lower than expected based on body composition. Furthermore, those who experienced the greatest

weight loss and maintenance had the greatest slowing of RMR, which was not associated with weight regain. According to the investigators, “Society and health professionals can stop blaming victims—laziness is not a factor in weight regain.”

Neural Factors

Obesity is also reported to be associated with an increased preference for, and consumption of, foods high in fat and sugar, driven by factors such as neural dopamine (10). People trying to reduce their intake of high-fat and sugar-containing foods report unpleasant physical and psychological sensations, including insatiable cravings, fatigue, and poor mood. With weight loss, a decrease in rewards from food intake occurs, resulting in neural dopamine signaling that drives an increased consumption to make up for the deficit (10).

Summary

We have reviewed evidence that biological mechanisms, including genetic factors, hormonal changes, adaptive thermogenesis, and neural factors, undermine weight loss effects and promote weight regain in individuals attempting even modest weight loss. These mechanisms appear to defend an individual's highest sustained body weight and point to the crucial importance of obesity prevention efforts for normal-weight and overweight individuals. Although it is likely that psychological and social issues also contribute to difficulties in maintaining weight loss, whether and how they do remain only speculation and require further research. Hopefully, reviews such as this will increase HCPs' awareness of the reasons individuals with obesity struggle to achieve and maintain weight loss. Hopefully, sharing this information with individuals struggling with the problem can relieve some of the guilt and frustration they often experience.

This brings us back to the topic of assisting individuals with diabetes in dealing with lifestyle decisions

related to weight issues. A collaborative approach is first and always the most important first step. Individuals must decide what they are willing and able to implement into their lifestyle. The focus of nutrition therapy for all individuals living with longer-duration type 2 diabetes is on reduced energy intake with an emphasis on nutrient-dense, fiber-rich foods, along with regular physical activity (21). Individuals need to be informed regarding the challenges of weight maintenance. It is important for them to understand that powerful biological mechanisms promote weight regain and that this is not a reflection of weak willpower. Together, HCPs and their clients need to continue monitoring progress and adjusting treatment strategies as necessary. It is hoped that, if individuals better understand the problems they face and treatments to address them, they will be better able to effectively manage their diabetes.

Duality of Interest

No potential conflicts of interest relevant to this article were reported.

References

- Ochner CN, Tsai AG, Kushner RF, Wadden TA. Treating obesity seriously: when recommendations for lifestyle confront biological adaptations. *Lancet Diabetes Endocrinol* 2015;3:232–234
- Phelan SM, Burgess DJ, Yeazel MW, Hellerstedt WL, Griffin JM, van Ryn M. Impact of weight bias and stigma on quality of care and outcomes for patients with obesity. *Obes Rev* 2015;16:319–326
- O'Brien KS, Puhl RM, Latner JD, Mir A, Hunter JA. Reducing anti-fat prejudice in preservice health students: a randomized trial. *Obesity (Silver Spring)* 2010;18:2138–2144
- Heymsfield SB, Wadden TA. Mechanisms, pathophysiology, and management of obesity. *N Engl J Med* 2017;376:254–266
- López-Lluch G. Mitochondrial activity and dynamics changes regarding metabolism in ageing and obesity. *Mech Ageing Dev* 2017;162:108–121
- Franz MJ, VanWormer JJ, Crain AL, et al. Weight-loss outcomes: a systematic review and meta-analysis of weight-loss

- clinical trials with a minimum of 1-year follow-up. *J Am Diet Assoc* 2007;107:1755–1767
- Franz MJ, Boucher JL, Ruten-Ramos C, VanWormer JJ. Lifestyle intervention outcomes in overweight and obese adults with type 2 diabetes: a systematic review and meta-analysis of randomized clinical trials. *J Acad Nutr Diet* 2015;115:1447–1463
- Bray MS, Loos RJJ, McCaffery JM, et al. NIH working group: using genomic information to guide weight management: from universal to precision treatment. *Obesity* 2016;24:14–22
- Locke AE, Kahali B, Berndt SI, et al. Genetic studies of body mass index yield new insights for obesity biology. *Nature* 2015;518:197–206
- Ochner CN, Barrios DM, Lee CD, Pi-Sunyer FX. Biological mechanisms that promote weight regain following weight loss in obese humans. *Physiol Behav* 2013;120:106–113
- Schwartz MX, Woods SC, Porte D Jr, Seeley RJ, Baskin DG. Central nervous system control of food intake. *Nature* 2000;202:661–671
- Leibel RL. The role of leptin in control of body weight. *Nutr Rev* 2002;60:S15–S19
- Jackman MR, Steig A, Higgins JA, et al. Weight regain after sustained weight reduction is accompanied by suppressed oxidation of dietary fat and adipocyte hyperplasia. *Am J Physiol Regul Integr Comp Physiol* 2008;294:R1117–R1129
- Gutzwiller JP, Goke B, Drewe J, et al. Glucagon-like peptide-1: a potent regulator of food intake in humans. *Gut* 1999;44:81–86
- Batterham RL, Le Roux CW, Cohen MA, et al. Pancreatic polypeptide reduces appetite and food intake in humans. *J Clin Endocrinol Metab* 2003;88:3989–3992
- Sumithran P, Prendergast LA, Delbridge E, et al. Long-term persistence of hormonal adaptations to weight loss. *N Engl J Med* 2011;365:1597–1604
- Camps SGJA, Verhoef SPM, Westerterp KR. Weight loss, weight maintenance, and adaptive thermogenesis. *Am J Clin Nutr* 2013;97:990–994
- Astrup A, Gotzsche PC, van de Werken K, et al. Meta-analysis of resting metabolic rate in formerly obese subjects. *Am J Clin Nutr* 1999;69:1117–1122
- Rosenbaum M, Hirsch J, Gallagher DA, Leibel RL. Long-term persistence of adaptive thermogenesis in subjects who have maintained a reduced body weight. *Am J Clin Nutr* 2008;88:908–912
- Fothergill E, Guo J, Howard L, et al. Persistent metabolic adaptation 6 years after “The Biggest Loser” competition. *Obesity* 2016;24:1612–1619
- Evert AB, Boucher JL, Cypress M, et al. Nutrition therapy recommendations for the management of adults with diabetes. *Diabetes Care* 2013;37:1544–1553