Sleep Well and Stay Slim: Dream or Reality?

The prevalence of obesity is increasing worldwide, with serious consequences for affected individuals, health care systems, and society. Because of the lack of effective interventions for obesity prevention, obesity is likely to continue to be a major public health challenge for many years to come. Once obesity occurs, the available medical treatment options include only a diminishing array of drugs and bariatric surgery. The key to successful weight loss and its maintenance is adoption of a healthy lifestyle through altering food selection, reducing calorie intake, and increasing physical activity (1). Unfortunately, many obese individuals do not successfully modify their lifestyle, and many who succeed initially do not maintain positive behavior changes and eventually regain weight. The barriers to maintaining healthy body weight are complex and include physiologic, psychological, and social factors. Emerging evidence points to sleep duration as another factor that influences weight (2). From a population perspective, sleep duration has decreased as obesity rates have risen (3). Both animal and human studies document physiologic links among sleep duration, circadian rhythms, and metabolism (4). Furthermore, geographically diverse studies including individuals of various ages suggest a link between short sleep duration and obesity (5).

However, most studies on sleep and weight are cross-sectional and thus are unable to determine which came first: the short sleep or the high weight (3, 6). One large population-based study provided insight into potential mechanisms, showing that shorter sleep was associated with higher circulating ghrelin levels and lower circulating leptin levels—hormonal changes usually seen in states of calorie deficit that could contribute to weight gain through alterations in food intake and energy expenditure (7). The stomach releases ghrelin to signal hunger, and adipocytes release leptin to signal the state of the body's fat stores. Both hormones act through the hypothalamus, the major homeostatic regulator that is well placed to integrate sleep with appetite and energy expenditure. After weight loss through calorie reduction, ghrelin levels are high and leptin levels are low, possibly contributing to rapid weight gain after resumption of less calorie-restricted eating. Rodent studies showed that sleep deprivation was associated with increased energy expenditure and hyperphagia (8). Further evidence for a link between sleep duration and metabolism comes from healthy volunteer studies in which acute partial sleep deprivation led to increased ghrelin levels, decreased leptin levels, and increased appetite (9). Of interest, reduced leptin associated with shorter sleep may be most pronounced in the presence of moderate calorie restriction (10).

In this issue, Nedeltcheva and colleagues (11) report a crossover study in which 10 sedentary, overweight volunteers who were otherwise healthy had sleep limited to 5.5 hours per night for another 14 days and 8.5 hours per night for another 14 days in random order. Participants restricted calorie intake during these sleep manipulations. Weight loss through calorie restriction was less from body fat and more from lean body mass in the 5.5-hour sleep group than the 8.5-hour sleep group. Fat oxidation was also lower in the sleep-deprived state. Acylated ghrelin (the active circulating ghrelin form) and hunger levels were also found to be higher with sleep deprivation. These results suggest differential effects of calorie restriction with sleep deprivation on fat storage and use. The authors speculate that the preferential loss of lean body mass could be related to the conversion of muscle protein to glucose to cater for the brain's increased demand for substrate. More detailed and larger metabolic studies are required to confirm this hypothesis.

These findings provide insight on why sleep deprivation interferes with the achievement and maintenance of healthy weight. First, insufficient sleep leads to hunger, making restricting calories difficult. Second, preferential loss of muscle to fat with insufficient sleep could compromise further weight loss and weight loss maintenance. Adequate sleep might be an important factor in successful weight loss, and perhaps sleep should be included as part of the lifestyle package that traditionally has focused on diet and exercise (5).

Although the study suggests an avenue to improved and successful weight loss, several important questions remain regarding the link between sleep and metabolism. Whether individuals adapt to sleep deprivation that lasts longer than 14 days is unknown. The study includes only 10 healthy participants and may not generalize to others, including those with comorbid conditions. A major problem with sleep laboratory studies is their applicability in real life, where multiple other factors influence a person's ability to maintain a diet. Nedeltcheva and colleagues (10) previously reported an association between sleep deprivation and high snack consumption, suggesting that increased wakefulness could influence body weight through increased opportunity to overeat.

There may be other mechanisms through which sleep duration influences metabolism. Nedeltcheva and colleagues (11) did not detect a change in energy expenditure in the sleep-deprived state, but subtle changes could result in weight gain over time. Sleep loss could result in daytime fatigue that could hamper attempts to increase physical activity. We have more to learn about the relationship between sleep duration and daily physical activity. It is also possible that sleep deprivation leads to poor decision making about diet choices. Of interest, Nedeltcheva and colleagues did not observe the significant change in leptin levels that was observed in previous studies (12), suggesting that we also have more to learn about leptin's role in the

interaction between sleep duration and metabolism. We also lack information about the stages of sleep that are most important to metabolism. Some studies suggest that slow-wave sleep loss is associated with metabolic alterations, whereas other studies suggest a role for rapid eye movement sleep (13, 14). Finally, increased body weight, even in the moderate range, is associated with increased sleep-disordered breathing, which even if subclinical might have physiologic effects on metabolism and weight loss.

Conducting careful human studies in the sleep laboratory is complicated. Yet, replicating these findings in the clinical arena is a critical next step (6, 15) in addressing important questions about sleep and body weight. Is it feasible to extend sleep duration in obese individuals who sleep only for short periods? If so, can patients sustain these changes, and will it improve the achievement and maintenance of healthy body weight? What is the optimal sleep duration, and should interventions target a particular stage of sleep? Is there a role for pharmacotherapy in achieving ideal sleep patterns? A systematic approach to answering these questions has the potential to identify new weapons in our armamentarium against obesity and turn the dream of achieving healthy body weight through sleep manipulation into reality.

Shahrad Taheri, MBBS, PhD
University of Birmingham, Birmingham Collaboration for Leadership in Health Research and Care, and Heartlands Biomedical Research Centre
Birmingham B9 5SS, United Kingdom

Emmanuel Mignot, MD, PhD
Stanford Sleep Medicine Center
Redwood City, CA 94063

Potential Conflicts of Interest: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M10-2045.

Requests for Single Reprints: Shahrad Taheri, MBBS, PhD, Heartlands Biomedical Research Centre, MIDRU Building, Heartlands Hospital, Bordesley Green East, Birmingham B9 5SS, United Kingdom; e-mail, S.Taheri@bham.ac.uk.

Current author addresses are available at www.annals.org.

Ann Intern Med. 2010;153:475-476.

References

1. **Wing RR, Phelan S.** Long-term weight loss maintenance. Am J Clin Nutr. 2005;82:222S-225S. [PMID: 16002825]
2. **Taheri S.** Sleep and metabolism: bringing pieces of the jigsaw together [Editorial]. Sleep Med Rev. 2007;11:159-62. [PMID: 17517354]
3. **Cizza G, Skarulis M, Mignot E.** A link between short sleep and obesity: building the evidence for causation [Editorial]. Sleep. 2005;28:1217-20. [PMID: 16295203]
4. **Maury E, Ramsey KM, Bass J.** Circadian rhythms and metabolic syndrome: from experimental genetics to human disease. Circ Res. 2010;106:447-62. [PMID: 20167942]
5. **Taheri S.** The link between short sleep duration and obesity: we should recommend more sleep to prevent obesity. Arch Dis Child. 2006;91:881-4. [PMID: 17056861]
6. **Taheri S, Thomas GN.** Is sleep duration associated with obesity—where do U stand? Sleep Med Rev. 2008;12:299-302. [PMID: 18603219]
7. **Taheri S, Lin L, Austin D, Young T, Mignot E.** Short sleep duration is associated with reduced leptin, elevated ghrelin, and increased body mass index. PLoS Med. 2004;1:e62. [PMID: 15602591]
8. **Rechtschaffen A, Bergmann BM, Everson CA, Kushida CA, Gilliland MA.** Sleep deprivation in the rat: X. Integration and discussion of the findings. 1989. Sleep. 2002;25:68-87. [PMID: 11833857]
9. **Spiegel K, Tasali E, Penev P, Van Cauter E.** Brief communication: sleep curtailment in healthy young men is associated with decreased leptin levels, elevated ghrelin levels, and increased hunger and appetite. Ann Intern Med. 2004;141:846-50. [PMID: 15583226]
10. **Nedeltcheva AV, Kilkus JM, Imperial J, Kasza K, Schoeller DA, Penev PD.** Sleep curtailment is accompanied by increased intake of calories from snacks. Am J Clin Nutr. 2009;89:126-33. [PMID: 19056602]
11. **Nedeltcheva AV, Kilkus JM, Imperial J, Schoeller DA, Penev PD.** Insufficient sleep undermines dietary efforts to reduce adiposity. Ann Intern Med. 2010;153:435-41.
12. **Spiegel K, Leproult R, L'hermite-Balériaux M, Copinschi G, Penev PD, Van Cauter E.** Leptin levels are dependent on sleep duration: relationships with sympathovagal balance, carbohydrate regulation, cortisol, and thyrotropin. J Clin Endocrinol Metab. 2004;89:5762-71. [PMID: 15531540]
13. **Liu X, Forbes EE, Ryan ND, Rofey D, Hannon TS, Dahl RE.** Rapid eye movement sleep in relation to overweight in children and adolescents. Arch Gen Psychiatry. 2008;65:924-32. [PMID: 18678797]
14. **Tasali E, Leproult R, Ehrmann DA, Van Cauter E.** Slow-wave sleep and the risk of type 2 diabetes in humans. Proc Natl Acad Sci U S A. 2008;105:1044-9. [PMID: 18172212]
15. **Cizza G, Marincola P, Mattingly M, Williams L, Mitler M, Skarulis M, et al.** Treatment of obesity with extension of sleep duration: a randomized, prospective, controlled trial. Clin Trials. 2010;7:274-85. [PMID: 20423926]

Current Author Addresses: Dr. Taheri: Heartlands Biomedical Research Centre, MIDRU Building, Heartlands Hospital, Bordesley Green East, Birmingham B9 5SS, United Kingdom.
Dr. Mignot: Stanford Sleep Medicine Center, 450 Broadway Street, Pavilion B, 2nd Floor, Redwood City, CA 94063.