

A New Challenge to Widely Held Views on the Role of Sleep

Philosophers, moralists, and scientists have been interested in sleep since ancient times. Although hypotheses and beliefs about the role of sleep have varied over the centuries, many have considered sleep to be an idle state or a sole function of the brain (1). However, suggestions of a link between sleep and metabolic functions can be found in early Roman medicine. Aulus Cornelius Celsus (circa 25 BCE to 50 ACE) argued in favor of “restricted sleep” for the treatment of extra weight, and Galen (129 to circa 216 ACE) listed “*somnux et vigilia*” (sleeping and waking) as important causes of illness (2).

With the turn of the 20th century, research about the effects of sleep on health risks has sharply increased. This scientific work is stimulating a public health debate that points to the declining trends in quality and quantity of sleep in modern society as contributing factors to ill health (1).

We spend approximately one third of our lifetime asleep, more as babies and children, settling into a pattern of approximately 7 to 8 hours per night in adulthood. Data suggest that modern society’s trends of longer work hours; more shift work; and 24-hour, 7-day-per-week availability of commodities have been accompanied by reduced sleep duration (1). Too little sleep is associated with adverse health outcomes that include total mortality (3), stroke and coronary heart disease (4), type 2 diabetes (5), hypertension (6), respiratory disorders (1), poor self-rated health (1), and obesity in adults and children (7).

Although the potential public health implications of a causal relationship between poor sleep and poor health would be far-reaching, observational studies do not prove causality. Short-term randomized clinical trials of manipulation of sleep duration support the hypothesis that sleep deprivation leads to impaired glucose tolerance and increased insulin resistance (8), increased appetite through changes in leptin and ghrelin levels (9), and reduced energy expenditure (10).

In this issue, Broussard and colleagues (11) report the results of a randomized, crossover clinical trial of sleep deprivation in 7 young, healthy volunteers. After a week of stabilization, the volunteers underwent, in random order and 4 weeks apart, 4 nights of normal sleep (8.5 hours) and 4 nights of sleep deprivation (4.5 hours). The researchers monitored sleep stage with polysomnography and adherence to bedtime schedules with actigraphy. Caloric intake and meals were kept constant throughout the study.

At the end of each study period, the participants had an intravenous glucose tolerance test to measure total body insulin sensitivity and a subcutaneous abdominal fat biopsy to isolate adipocytes. Researchers then exposed adipocytes in vitro to incremental insulin concentrations to measure the ability of insulin to increase the phosphorylation of Akt, an important step in the insulin-signaling pathway.

The results show that sleep deprivation was associated with a 30% reduction in phosphorylation of Akt. This finding indicated reduced peripheral insulin response and was paralleled by a reduction in total body insulin sensitivity. To our knowledge, this is the first clinical study linking sleep restriction to an alteration of a molecular metabolic pathway.

The authors deserve commendation for a study that is a valuable contribution to the understanding of the causal pathways by which reduced sleep duration may directly contribute to diabetes and obesity. The study used a strictly controlled experimental design with a crossover phase to minimize between-participant variability. Measures of sleep were objective and were performed in standardized conditions. Finally, the effect size of a 30% reduction in peripheral insulin sensitivity is biologically relevant and, if sustained over longer periods and shared by other tissues, could be of clinical and public health relevance for understanding the development of diabetes and obesity.

In such a difficult field of research, limitations are unavoidable and 4 issues deserve consideration. The experimental model compares the effect of an average 3.5-hour difference in sleep duration per day (equivalent to an accumulated sleep debt of 14 hours over 4 days). This is a large difference accrued within a short period, and it is not clear to what degree the effects seen under such conditions would be reproduced if sleep deprivation were less severe but extended over a longer period. It is possible that acute and chronic sleep loss may exert different effects on metabolism as observed with the effect of sleep on human performance (12).

Substantial interparticipant variation in the effect was reported in the 7 persons studied. Although this does not affect statistical power, it may indicate differences in susceptibility.

Prolonged sleep restriction combined with disruption of circadian cycles exerts adverse metabolic effects on resting metabolic rate and postprandial plasma glucose and insulin secretion (13). However, how well the protocol used in this study controlled for circadian cycles is unclear.

Finally, Broussard and colleagues do not specify whether they standardized participant exposure to light. Whether the additional 4 hours per night that participants spent awake during periods of sleep deprivation were spent in darkness could influence the observed results. Thus, it is difficult to assess whether the reported differences were due to reduced sleep or to extended periods of light exposure. Duration of exposure to light (or darkness) regulates hormone secretion (14) and, at least in animal models, affects the sensitivity of adipocytes to sympathetic stimulation and induces changes in lipolysis (15, 16).

Nonetheless, Broussard and colleagues' study substantially challenges the traditional views that the primary purpose of sleep is confined to restorative effects on the central nervous system. These results point to a much wider influence of sleep on bodily functions, including metabolism, adipose tissue, cardiovascular function, and possibly more. These observations support the quest for ways to reduce the external threats to sleep duration and quality as a strategy to improve the health of both individuals and society. Last, it seems that Celsus may have been wrong: He should have argued in favor of "prolonged sleep" for the treatment of extra weight.

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