Obesity, genes, and sleep habits

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Obesity is a multifactorial health problem that remains an object of major preoccupation, partly because of the difficulty in deriving effective prevention and treatment strategies from recent research on its etiology. In this regard, it is still valid to consider that obesity is the consequence of a positive energy-lipid balance. However, it is also relevant to emphasize that the firstlaw of thermodynamics, which underlies this issue, is not so informative about the cause of obesity. Current mechanistic and clinical research has highlighted the potential impact of unsuspected environmental factors that might contribute more to altering energy balance than the traditionally considered determinants of obesity (i.e., insufficient physical activity and suboptimal diet). These factors include short sleep duration, which promotes hormonal changes related to excess energy intake (1, 2), reduced energy expenditure (3), and a state of fatigue associated with reduced physical activity (4). Accordingly, population studies repeatedly showed that short sleepers are at greater risk of excess body weight (5, 6). Evidence also shows that long sleepers (e.g., adults who report ≥9 h sleep/d) are more prone to overweight (6).

Research in genetics has also contributed to innovation in obesity by showing the existence of genetic-environment interaction effects that influence the predisposition to gain or to lose body fat in response to lifestyle changes. For instance, overfeeding in monozygotic twins resulted in a significant within-pair similarity in body fat changes over time, suggesting that heredity can modify the response of body energy stores to hyperphagia (7). More recently, the advent of genomewide association studies has enabled the identification of several genetic variants that show robust associations with obesity-related phenotypes, such as BMI (8) and waist circumference (WC) (9). The discovery of these genomewide association study–derived genetic markers led to a new approach to the exploration of gene-environment interaction effects with the use of genetic risk scores as a global measure of genetic susceptibility, which considerably reduces the burden of multiple testing associated with single-marker analyses. In this issue of the Journal, Celis-Morales et al. (10) considered all of these research developments together in a large cohort study that involved the testing of 119,679 white European adults participating in the UK Biobank. The outcome variables considered were BMI and WC, whereas the independent predictor marker was a genetic profile risk score (GPRS). As expected, a significant relation was observed between the outcome variables and GPRS. The results also showed that sleep duration modulated this relation. Specifically, the association between GPRS and BMI or WC was more pronounced in short (<7 h/d) and long (>9 h/d) sleepers than in normal sleepers (7–9 h/d). From a scientific standpoint, this finding is novel and provides evidence for the first time, to our knowledge, that sleep-related behaviors influence genetic susceptibility to obesity.

Beyond its contribution to scientific innovation, this study has important clinical implications. First, it adds to the evidence that some individuals are at increased risk of obesity because they inherited susceptibility genes. Second, the reported results provide a different facet of the gene-environment interaction. As indicated above, this concept has traditionally been used to describe the influence of single genes on the body’s response to environmental and lifestyle changes. This vision is extended by the results of the present study, which shows that an environmental factor such as sleep duration can modify the relation between genetic susceptibility, as assessed by a GPRS, and energy balance. Third, this study contributes to proof-of-concept of personalized medicine in obesity by providing evidence that, for some individuals, changes in sleep-related behaviors might be relevant to partly compensate for an increased genetic susceptibility to obesity.

Globally, the study by Celis-Morales et al. (10) offers interesting perspectives toward predictive and personalized medicine. Indeed, the modulation of the genetic risk of obesity by sleep habits suggests that obesity management will be enriched in the near future by the documentation of an interaction between susceptibility genes and a better understanding of environmental effects on energy balance.

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REFERENCES

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