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# A single night of partial sleep deprivation induces insulin resistance in multiple metabolic pathways in healthy subjects - Evidence review

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## 1. ABSTRACT

The analyzed study evaluated whether a single night of sleep restricted to four hours could alter insulin sensitivity in healthy adults. In nine participants, compared to a night of normal sleep, the restriction reduced the ability of peripheral tissues to utilize glucose in response to insulin and decreased the suppression of hepatic glucose production.The publication contributes to the narrative of "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R. Panzironi, according to which insufficient sleep can be accompanied by insulin resistance. However, the available material does not report cortisol measurements: the study demonstrates metabolic alteration, not that it is caused by an increase in this hormone. Independent experimental studies confirm the worsening of insulin sensitivity after sleep restriction, including reduced signaling of the AKT pathway in adipose tissue. However, a meta-analysis indicates that the effects may vary according to the tissue, the measurement method, and the type of sleep disturbance.

ONLINE ARTICLE

ARTICLE INFORMATION

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## 2. ANALYZED STUDY

The research question was simple yet relevant: can just one night of reduced sleep temporarily make the body less sensitive to insulin? The hypothesis was that partial sleep deprivation would impair both the liver's response, which normally reduces glucose production when insulin increases, and the response of peripheral tissues, especially muscle and adipose tissue, which normally absorb glucose from the blood.The relevance to sections 4.14 and 4.15 of "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R. Panzironi therefore concerns the segment of insufficient sleep reduced insulin efficacy insulin resistance. The study analyzed directly documents this physiological segment in healthy individuals. However, it does not measure cortisol and does not analyze the proteins of the PI3K/AKT/mTOR pathway; therefore, it cannot demonstrate that any variation in cortisol is the cause of insulin resistance, nor can it identify the precise molecular step involved.

## 3. MATERIALS AND METHODS OF THE ORIGINAL STUDY

The study used a within-subject experimental design: nine healthy volunteers, five men and four women, were evaluated once after a normal night's sleep and once after a night of restricted sleep. In the normal condition, sleep was permitted from 11:00 PM to 7:30 AM; in the restricted condition, it was permitted from 1:00 AM to 5:00 AM, i.e., for four hours.Sleep duration and characteristics were monitored using polysomnography, a recording that measures sleep, breathing, and brain activity. Insulin sensitivity was assessed using a hyperinsulinemic-euglycemic clamp, a procedure in which insulin is administered while maintaining stable glycemia via intravenous glucose: the amount of glucose required helps estimate how effectively the body responds to insulin. Isotopically labeled glucose was also used to distinguish infused glucose from that produced by the liver.The clamp was performed from 11:30 AM to 2:30 PM. The primary variables were endogenous glucose production, i.e., glucose produced by the body primarily by the liver, the rate of glucose utilization by tissues, and the glucose infusion rate. Detailed inclusion and exclusion criteria, recruitment period, order of experimental conditions, and the complete statistical method are not reported in the available material, which consists only of the abstract.

## 4. RESULTS

Sleep restriction was effectively achieved: average sleep time went from 454 ± 9 minutes on a normal night to 226 ± 11 minutes on a restricted night, a statistically significant reduction ($P<0.0001$). In the morning, before the clamp, no significant differences emerged in glycemia, insulin, non-esterified fatty acids, or endogenous glucose production. This means that the metabolic difference was not evident in the simple baseline values measured in the abstract.During the clamp, when insulin is expected to suppress glucose production by the liver, endogenous production remained higher after the short night: 4.4 ± 0.3 versus 3.6 ± 0.2 micromoles per kilogram of lean body mass per minute ($P=0.017$). In practical terms, the liver responded less effectively to insulin, a sign of hepatic insulin resistance.Peripheral tissues also utilized less glucose in response to insulin. The glucose disposal rate dropped from 40.7 ± 5.1 to 32.5 ± 3.6 micromoles per kilogram of lean body mass per minute after sleep restriction ($P=0.009$). Consistently, the glucose infusion rate required to maintain stable glycemia decreased by approximately 25% ($P=0.001$): less glucose needed to be provided because the tissues were taking it up less efficiently.During the clamp, plasma non-esterified fatty acids increased from 57 ± 4 to 68 ± 5 micromoles per liter after reduced sleep ($P=0.005$). Since higher levels of these circulating fats can hinder insulin action, the data is biologically consistent with lower insulin sensitivity. The available material does not report morning, evening, or urinary cortisol measurements.

## 5. INTERPRETATION

The main result indicates that even a single very short night of sleep can temporarily reduce the efficiency with which insulin regulates glucose. The effect was observed in two fundamental sites: the liver, which continued to produce more glucose despite the presence of insulin, and peripheral tissues, which removed less glucose from the blood.This is the specific mechanism documented by the study analyzed: acute sleep reduction decreased hepatic and peripheral insulin sensitivity. This is an experimental result in humans rather than a simple observational

association; however, it is derived from only nine healthy participants and describes an acute response. It does not prove that one short night causes diabetes, nor does it quantify long-term risk.The book's chapters present a broader chain linking insufficient sleep, cortisol, and the insulin pathway. The publication subject to this Evidence Review precisely supports the final part of the chain, namely insulin resistance following partial sleep deprivation. It does not prove the step of insufficient sleep  increased cortisol, because cortisol is not reported in the available abstract. Nor does it demonstrate a direct reduction in PI3K, AKT, or mTOR, which are proteins that transmit insulin signals inside the cell.

## 6. INDEPENDENT SUPPORTING EVIDENCE

Mechanistic confirmation in humans comes from a randomized crossover study conducted on seven healthy young adults. After four days of 4.5 hours in bed per night, compared to four days of 8.5 hours, adipose cells obtained via subcutaneous biopsy required nearly triple the insulin concentration to reach half the phosphorylated AKT response. AKT is a protein that helps transmit the insulin message inside the cell; its reduced activation indicates that insulin signaling is becoming less efficient. The overall area of the cellular response was also reduced by 30%, in parallel with a reduction in whole-body insulin sensitivity [1]. This study confirms the narrative regarding the reduced efficacy of peripheral insulin signaling, but it primarily concerns adipose tissue and a very small sample.A second randomized crossover study evaluated 14 adults after five nights of four hours in bed or eight hours in bed. The restriction reduced whole-body insulin sensitivity by 25% and peripheral sensitivity by 29%; however, hepatic sensitivity did not decrease in a statistically significant manner. In the same experiment, 24-hour urinary free cortisol increased by 21% and fasting non-esterified fatty acids increased by 62% [2]. This result reinforces both the relationship between short sleep and peripheral insulin resistance and the plausibility of hormonal stress involvement, without, however, proving that cortisol is the sole or primary cause of the effect.A systematic review with meta-analysis of 35 randomized trials synthesized the effects of sleep manipulation on indicators of insulin sensitivity. Sleep duration restriction reduced insulin sensitivity as assessed by glucose tolerance tests, intravenous tests, and the HOMA-IR index, an indicator based on fasting glucose and insulin. Whole-body sensitivity measured by clamp was also found to be reduced. However, the analysis did not detect a significant effect on peripheral sensitivity across all combined studies [3]. This apparent discrepancy does not invalidate individual experimental studies, but shows that the intensity of the effect, metabolic site, and measurement method can vary.

## 7. CONFLICTING EVIDENCE

No directly conflicting evidence sufficiently relevant to the main result of the analyzed study—namely, the onset of insulin resistance after a single night of partial sleep deprivation—has been identified. However, there are elements that call for caution. In a meta-analysis of randomized trials, sleep restriction reduced overall insulin sensitivity but did not show a statistically significant reduction in peripheral sensitivity when the available data were combined [3].This difference may depend on non-overlapping protocols: duration of restriction, number of nights, age and sex of participants, controlled or ad libitum diet, the method used to measure insulin resistance, and the distinction between liver, muscle, and adipose tissue. Furthermore, the review found that sleep fragmentation did not have a significant effect in the quantitative synthesis, even though negative effects have been described in individual studies. Therefore, not all forms of sleep disturbance necessarily produce the same metabolic effect or an effect of the same magnitude.

## 8. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

The table distinguishes the publication subject to the review from the independent research used to evaluate the same biological narrative.

### Quadro comparativo

| Reference | Study type | Population or model | Main result | Direction of evidence | Strength of evidence |
|---|---|---|---|---|---|
| Original study | Crossover experimental | 9 healthy adults; one normal night and one night with four hours of sleep | Restriction increased hepatic glucose production during the clamp and reduced peripheral glucose utilization. | direct confirmation | moderate |
| [1] | Crossover RCT | 7 healthy young adults; subcutaneous adipocytes and systemic metabolic test | Four days of reduced sleep decreased AKT-mediated insulin response in fat cells and overall insulin sensitivity. | direct confirmation | moderate |
| [2] | Crossover RCT | 14 adults; five nights with four or eight hours in bed | Reduced sleep decreased overall and peripheral insulin sensitivity and increased free urinary cortisol. | direct confirmation | moderate |
| [3] | Systematic review and meta-analysis of RCTs | 35 randomized studies; 21 included in the meta-analysis on sleep restriction | Restriction reduced several indicators of insulin sensitivity, but the peripheral effect was not significant in the combined synthesis. | discordant evidence | high |

## 9. SINTESI EDITORIALE E CONCLUSIONI

### CONCLUSIONS

The analyzed study shows that, in nine healthy adults, one night of sleep restricted to four hours was followed by lower insulin sensitivity in both the liver and peripheral tissues. This result is consistent with independent experimental studies that document a worsening of the insulin response and, in adipose tissue, reduced AKT activation.The narrative that insufficient sleep can contribute to insulin resistance is therefore well-supported under acute experimental conditions. However, it is necessary to distinguish this conclusion from the claim that cortisol is the direct cause of the effect: the original study did not measure it, and available evidence suggests a possible contribution, not an exclusive causal demonstration. Further confirmation is needed in larger samples, in women and men of different ages, and under conditions of prolonged sleep restriction.

Aggiornato al 24/11/2026. Questo contenuto riflette una sintesi divulgativa delle evidenze scientifiche al momento della pubblicazione e non sostituisce il parere medico.

## 10. TRANSPARENCY AND SCIENTIFIC RESPONSIBILITY

Artificial Intelligence was used solely as a tool for editorial and documentary support. All content, interpretations, bibliographic citations and conclusions have been verified, reviewed and approved by the author, who assumes full scientific responsibility for them.

The manuscript was also subjected to independent peer review prior to publication.
To ensure the greatest transparency, the complete history of the article, including the dates of submission, revision, acceptance and publication, as well as information on the peer review process, is available on the dedicated Article History page.

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