LIFE Science Hub
JOURNAL OF SCIENCE
EXPANDING KNOWLEDGE ABOUT NUTRITION AND HEALTH

ORIGINAL RESEARCH
ISSN 2845-7501

Insulin signaling in skeletal muscle and whole-body glucose metabolism after acute sleep restriction in healthy men - Evidence review

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1. ABSTRACT

The analyzed study evaluated whether two nights of sleep restricted to 50% of the habitual duration would alter how the body responds to glucose and insulin. Ten young, healthy men completed both conditions in a randomized crossover design. After sleep restriction, blood glucose during the oral glucose tolerance test did not increase, but the insulin required to maintain it was higher, and the Matsuda index, an indicator of insulin sensitivity, decreased by 18.6%.In paragraph 4.15 of "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R. Panzironi, the publication contributes to the narrative that short-term sleep restriction can early promote insulin resistance even in healthy individuals. Independent studies confirm the reduction in insulin sensitivity after sleep loss; however, data on the direct involvement of the PKB/Akt pathway in skeletal muscle remain inconclusive. The conclusion is therefore moderately supported at the systemic level and preliminary at the muscular level.

ONLINE ARTICLE

ARTICLE INFORMATION

Published: November 20, 2026
Updated: November 20, 2026

DOI 10.5281/zenodo.24392009

MISSION

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Free from political, industrial and commercial influence, the journal stands as an authoritative and independent editorial space, dedicated to promoting scientific culture, professional development and the growth of health awareness among the public.

2. ANALYZED STUDY

The research question was whether acute sleep restriction would reduce whole-body insulin sensitivity and whether this impairment would be accompanied by reduced activation of PKB, also known as Akt, in skeletal muscle. PKB/Akt is a protein that transmits part of the insulin signal within the cell and promotes the entry of glucose into muscle fibers.The hypothesis was biologically plausible: after a meal or a glucose load, muscle is one of the primary tissues that removes glucose from the blood. If the muscle responds less to insulin, the pancreas may need to produce more insulin to keep glycemia within similar limits. This is the relevant point for the book chapter: a short period of sleep loss can early on alter the systemic insulin response even without an immediate increase in glycemia.The study can demonstrate short-term metabolic differences in a small group of healthy men subjected to an experimental protocol. It cannot establish that two nights of reduced sleep cause diabetes, nor can it prove that the change in PKB in the muscle is the mechanism responsible for the entire reduction in insulin sensitivity.

3. MATERIALS AND METHODS OF THE ORIGINAL STUDY

A randomized crossover study was conducted: the same participants underwent both conditions, separated by three weeks. Ten healthy, non-smoking men, aged between 18 and 40, with a regular habitual sleep duration of 7-9 hours, completed the protocol. Subjects with sleep disorders, recent shift work, travel across time zones, inflammatory or metabolic diseases, and medications capable of interfering with metabolism were excluded.In one condition, participants slept for two nights for a duration close to their habit; in the other, they slept for two nights at 50% of their habitual duration. Sleep was monitored using wrist actigraphy, a device that estimates sleep and wakefulness based on movement. Nutrition for the preceding 48 hours was provided by the researchers and repeated in both conditions. Participants were asked to avoid intense exercise, caffeine, and alcohol.On the morning after the second night, while fasting, an OGTT (oral glucose tolerance test) was performed: participants ingested 82.5 g of dextrose, and blood samples were taken for up to 120 minutes. Glycemia, insulinemia, area under the curve, and the Matsuda index were measured. The latter estimates insulin sensitivity using glucose and insulin levels detected during the OGTT: a lower value indicates reduced insulin sensitivity. Biopsies of the vastus lateralis muscle were also collected before the test and after 30 and 120 minutes to measure PKB activity. For the PKB analysis, one sample was excluded due to technical issues, and the analysis involved nine participants.

4. RESULTS

Sleep restriction was effectively achieved. The average sleep duration was 442 ± 78 minutes in the control condition and 235 ± 34 minutes in the restriction condition, with a statistically significant difference, $P < 0.001$.The most important result for the reader is that blood glucose remained similar, but the body had to produce more insulin. Fasting glycemia was 4.92 ± 0.10 mmol/L in the control and 5.02 ± 0.06 mmol/L after restriction; there were no significant differences in glycemia during the OGTT or in the area under the glucose curve. Conversely, insulin was higher after restriction at 15 minutes, 59.1 ± 9.0 versus 48.5 ± 9.5 μIU/mL, $P = 0.031$, and at 45 minutes, 83.9 ± 10.2 versus 67.3 ± 10.8 μIU/mL, $P = 0.028$.The area under the insulin curve increased by 14% after reduced sleep, 8068 ± 901 versus 7069 ± 1018, $P = 0.013$. In parallel, the Matsuda index decreased from 4.19 ± 0.71 to 3.41 ± 0.51, a reduction of approximately 19%, $P = 0.010$. In simple terms, for the same glycemic response, a greater secretion of insulin was required: a picture consistent with an acute reduction in whole-body insulin sensitivity.In the muscle, PKB activity increased after the glucose load in both conditions. After habitual sleep, it increased on average by 2.7 times at 30 minutes; after restriction, it increased by 1.5 times. The difference in the change did not reach the conventional threshold of statistical significance, $P = 0.098$. At 120 minutes, the increase was 1.9 times in the control and 1.4 times after restriction, $P = 0.087$. These data indicate a trend toward a lower muscle insulin signaling response, rather than a conclusive demonstration of PKB inhibition.

5. INTERPRETATION

The systemic result is consistent with an early form of insulin resistance: the body temporarily maintains blood glucose at similar levels by increasing the amount of circulating insulin. This compensation does not equate to diabetes and does not imply that glycemia must necessarily increase after a few nights of reduced sleep. However, it does indicate that metabolic control may become less efficient.The publication subject to the Evidence Review directly supports the segment of the book's narrative regarding the early reduction in insulin sensitivity following brief sleep restriction. The most robust finding is the decrease in the Matsuda index associated with an increase in insulin during the OGTT. The data on muscle PKB/Akt, on the other hand, is exploratory: the observed differences were in the expected direction, but were not statistically significant and were based on nine evaluable biopsies.The distinction is important. The proposed chain can be summarized as reduced sleep less efficient insulin response greater need for insulin to control glucose. The analyzed study documents the central step in the whole organism well; it does not definitively prove that skeletal muscle, through PKB/Akt, is the primary site or mechanism of the alteration.

6. INDEPENDENT SUPPORTING EVIDENCE

Initial direct evidence comes from a crossover study on nine healthy adults, five men and four women. After just one night with four hours available for sleep, compared to a night of 8.5 hours, insulin sensitivity—measured using the hyperinsulinemic-euglycemic clamp, the experimental gold standard—decreased by 25%. Peripheral glucose uptake also decreased by 20%, while endogenous glucose production increased by 22%. This data confirms that even a brief, partial loss of sleep can impair the insulin response before significant changes in fasting glycemia necessarily appear [1]. The main limitation is the very small sample size.A second randomized crossover study added a mechanistic piece of evidence in human peripheral tissue. Seven healthy young adults spent four nights with 4.5 hours in bed and four nights with 8.5 hours, with controlled diet and activity. After restriction, whole-body insulin sensitivity decreased by 16%, P = 0.02. In adipose cells obtained via biopsy, the phosphorylated AKT response—the activated form of the insulin signal—was reduced: the response area was 30% lower, P = 0.01, and it required nearly triple the amount of insulin to achieve half of the maximum response [2]. While this does not directly confirm the findings in muscle, it makes the hypothesis that reduced sleep may weaken insulin-dependent signals in peripheral tissues biologically consistent.In a study conducted on 20 healthy men, seven nights with five hours in bed reduced insulin sensitivity by 20 ± 24% according to an intravenous glucose tolerance test, P = 0.001, and by 11 ± 5.5% according to a clamp, P < 0.04 [3]. The longer duration of the intervention compared to the analyzed study reinforces the consistency of the effect's direction. However, the protocol was conducted in a controlled inpatient setting and does not allow for a direct estimation of the effect of habitually reduced sleep in the general population.A systematic review with meta-analysis of randomized trials synthesized 35 eligible articles, including 21 studies on sleep restriction in the meta-analysis. Overall, sleep restriction reduced insulin sensitivity indices measured via OGTT, intravenous tests, and clamps. However, the review noted results dependent on the method and the type of sleep manipulation: for peripheral sensitivity, the limited number of available studies did not show a statistically clear overall effect [4]. This synthesis supports the general narrative but limits the certainty regarding the specific mechanism in individual tissues.

7. CONFLICTING EVIDENCE

No directly conflicting evidence of sufficient relevance has been identified regarding the primary finding that experimental sleep restriction can reduce overall insulin sensitivity in healthy adults. However, there are elements that require caution when extending this result to every metabolic parameter and every tissue.The available systematic review and meta-analysis found heterogeneity among protocols, measurement methods, and types of sleep disturbance. While it found an overall unfavorable effect on insulin sensitivity indices, it did not observe a statistically defined global effect on peripheral sensitivity in the few studies that measured it specifically [4]. Furthermore, in the analyzed study,

glycemia did not increase, and the alteration of muscle PKB was not statistically significant. These elements do not contradict the systemic reduction in insulin sensitivity, but they show that insulin compensation, the tissue involved, and the magnitude of the effect depend on the experimental context.

8. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

The table distinguishes the results observed in the study covered by the review from the independent publications used to evaluate the same narrative.

Quadro comparativo

Reference	Study type	Population or model	Main result	Direction of evidence	Strength of evidence
Original study	Randomized crossover	10 healthy men; PKB assessed in 9 muscle biopsies	Two nights at 50% of habitual sleep increased insulin and reduced the Matsuda index; muscle PKB tended to be less responsive	direct confirmation	moderate
[1]	Experimental crossover	9 healthy adults	One night with four hours of sleep reduced insulin sensitivity by 25% and peripheral glucose uptake by 20%	direct confirmation	moderate
[2]	Crossover RCT	7 healthy young adults; adipocytes from biopsy	Four nights of restriction reduced systemic sensitivity by 16% and cellular Akt response by 30%	biologically consistent evidence	moderate
[3]	Controlled experimental study	20 healthy men	Seven nights with five hours in bed reduced insulin sensitivity by 11-20%, depending on the measurement method	direct confirmation	moderate
[4]	Systematic review and meta-analysis of RCTs	35 articles; 21 sleep restriction studies in the meta-analysis	Overall unfavorable effect on insulin sensitivity indices, with uncertainty regarding specific peripheral sensitivity	discordant evidence	moderate

9. SINTESI EDITORIALE E CONCLUSIONI

CONCLUSIONS

The study analyzed shows that two nights of sleep reduced by 50% can decrease overall insulin sensitivity in healthy young men, even when glycemia during the glucose test remains similar. The result is consistent with a higher demand for insulin to maintain glycemic balance.Independent literature quite robustly confirms that experimental sleep restriction reduces insulin sensitivity in humans. The hypothesis that this effect depends on an alteration of the PKB/Akt pathway in peripheral tissues is supported primarily at a mechanistic level. In skeletal muscle, the data remains preliminary and requires larger studies with more precise measurements and more diverse participants.

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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