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Impact of sleep and sleep disorders on the activity of the hypothalamic-pituitary-adrenal axis - A review of the evidence

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1. ABSTRACT

The analyzed publication is a narrative review examining how sleep, awakenings, sleep loss, and circadian rhythm misalignment affect the hypothalamic-pituitary-adrenal axis, the hormonal system that regulates the production of cortisol. The work concludes that sleep onset tends to temporarily reduce cortisol secretion, while awakening and sleep loss can alter its daily profile. However, the authors note inconsistent results across total sleep deprivation studies.In section 4.15 of "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R. Panzironi, the study contributes to the narrative that prolonged wakefulness can alter the cortisol rhythm, with increases occurring primarily in the evening. Independent experiments confirm increases in evening cortisol following acute or repeated sleep restriction and show concurrent worsening of insulin sensitivity. However, a recent meta-analysis finds that the average effect of acute deprivation on cortisol is not statistically significant across all protocols. The most prudent conclusion is that the alteration exists under specific experimental conditions, but it is not identical in all people, at different times, or across various measurement methods.

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MISSION

LIFE Science Hub – Journal of Science was founded with the aim of making scientific knowledge accessible without giving up methodological rigour, quality of sources and authoritativeness of content. The journal promotes the dissemination of knowledge in the health, nutrition, medical and longevity sciences, building a bridge between the world of research and society.

Through articles, reviews, in-depth analyses and expert contributions, the Journal champions evidence-based medicine and science, fostering a correct interpretation of scientific data and countering misinformation. Every piece of content is developed with the aim of translating the complexity of research into understandable, useful and applicable information, while keeping intact the principles of accuracy, transparency and scientific independence.

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 to understand to what extent sleep and its disturbances modify the activity of the hypothalamic-pituitary-adrenal axis, often abbreviated as the HPA axis (the system that connects the brain, pituitary gland, and adrenal glands in the stress response). The general hypothesis was that sleep is not merely a passive period, but contributes to regulating cortisol secretion in conjunction with the circadian rhythm, which is the biological system that organizes many functions over a twenty-four-hour period.The relevance to the book's section is specific. In “The Choice to Live in Health or Illness” by Dr. A. Colonnese and R. Panzironi, the publication is cited to support the claim that twenty-four consecutive hours of wakefulness can alter the cortisol rhythm and increase its levels during the evening and night. The analyzed study documents, through a synthesis of the available literature, that sleep loss can increase cortisol, especially in the late afternoon and evening, but it also reports divergent results following total deprivation. It is therefore not an original experiment on a single sample and cannot prove that every person deprived of sleep for twenty-four hours will necessarily develop the same increase in salivary cortisol.

3. MATERIALS AND METHODS OF THE ORIGINAL STUDY

The publication is a narrative review of sleep physiology and the HPA axis, not a clinical trial conducted directly by the authors on new participants. The text describes human studies that used protocols of total sleep deprivation, partial restriction of time spent in bed, shifting of sleep and wake times, electroencephalographic sleep recording, and repeated measurements of cortisol in blood or saliva.The review distinguishes the effects of the circadian clock from those of sleep by using, in the cited works, controlled conditions such as dimmed light, standardized posture, regular meals, and frequent sampling. The authors also discuss studies on insomnia, depression, Cushing's syndrome, and sleep-disordered breathing. A systematic bibliographic search strategy, formal inclusion and exclusion criteria, risk of bias assessment, and meta-analysis are not reported in the available material.

4. RESULTS

The main physiological message is that cortisol does not remain constant: it normally reaches low levels around midnight, rises in the second half of the night, and increases further near waking. The onset of sleep exerts a temporary inhibition of cortisol secretion, while nocturnal awakenings and final awakening are associated with a transient or more prolonged increase.For the book's narrative, the most relevant result concerns sleep loss. The review reports that several studies on total sleep deprivation have observed higher cortisol levels during the night of wakefulness and, when wakefulness continued, in the following afternoon or evening. However, it also reports studies showing no detectable variations or a slight reduction in cortisol after one or more sleepless nights. The authors attribute some of these differences to non-overlapping protocols, physical activity and posture that were not always controlled, insufficient frequency of blood sampling, and the possible presence of unidentified short naps.The review also describes an experiment of repeated partial restriction: six nights with four hours in bed in eleven young men were associated with higher cortisol in the afternoon and early evening, as well as a delay of about an hour and a half in the start of the daily phase of low secretion. The text emphasizes that even a modest increase in evening cortisol, if recurrent, could contribute to metabolic overload; however, this is a pathophysiological interpretation and not the demonstration of a clinical disease.

5. INTERPRETATION

In simple terms, sleep helps keep cortisol within an orderly temporal profile. When sleep is reduced or eliminated, the evening shutdown phase of the stress axis can be delayed: cortisol therefore remains higher at a time when it should habitually decrease. This is the segment of the biological chain actually documented by the publication that is the subject of the Evidence Review.The possible metabolic link is plausible because cortisol promotes the availability of glucose in the blood and, if persistently elevated, can hinder the action of insulin in some tissues. However, the study analyzed does not prove that the temporary increase in cortisol caused by a single sleepless night is

the sole cause of insulin resistance. Sleep loss simultaneously alters sympathetic activity, diet, movement, light exposure, and circadian rhythms. Therefore, cortisol should be considered a possible hub of the response, not the only explanation for the metabolic effects.

6. INDEPENDENT CONFIRMING EVIDENCE

A controlled experiment on young men compared normal sleep, partial sleep deprivation, and total sleep deprivation. After a night of reduced sleep, plasma cortisol between 6:00 PM and 11:00 PM increased by 37% compared to the previous day; after total deprivation, the increase was 45%. In both conditions, the onset of the low cortisol secretion phase was delayed by at least one hour. This study directly confirms the section of the book regarding the evening increase following acute sleep loss, although it measured cortisol in plasma rather than saliva [1].A second experiment, conducted on eleven young men after six nights with four hours in bed compared to six nights with twelve hours in bed, found an increase in evening cortisol and a reduction in glucose tolerance. The data support a chain consistent with the paragraph: repeated sleep restriction, greater evening activation of the stress axis, and worsening of glucose regulation. However, the small sample size, consisting only of young men, limits the generalizability of the results to other populations [2].Sleep quality appears to be relevant beyond its duration. In eleven healthy volunteers, two nights of experimentally fragmented sleep reduced insulin sensitivity—that is, the efficiency with which the body responds to insulin—and increased morning cortisol. The insulin sensitivity index decreased from 5.02 to 3.76 mU/L–1min–1 ($P<0.0001$). While this does not specifically confirm the evening increase after twenty-four hours of wakefulness, it reinforces the biologically consistent link between disturbed sleep, activation of the stress axis, and impaired glucose metabolism [3].

7. CONFLICTING EVIDENCE

A systematic review with meta-analysis of twenty-four studies evaluated the effect of acute sleep deprivation on cortisol. In the twenty-one crossover design studies, in which the same participants underwent both conditions, the overall effect was not statistically significant: standardized mean difference 0.18, 95% confidence interval from –0.11 to 0.45; $P=0.208$. Even in the three randomized studies, the mean effect was not statistically significant.However, the same meta-analysis found higher cortisol levels after deprivation when the measurement was performed in serum and when multiple measurements over time were available. This evidence does not invalidate the experiments that observed evening increases, but it indicates that the response depends on the biological sample, the time of day, the duration of wakefulness, experimental controls, and individual variability. The passage in the book should therefore be interpreted as a possible effect documented in specific protocols, not as an invariable response to prolonged wakefulness [4].

8. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

The table distinguishes the publication subject to the review from the independent research used to evaluate the passage in the book.

Quadro comparativo

Reference	Study type	Population or model	Main result	Direction of evidence	Strength of evidence
Original study	Narrative review	Literature on humans and experimental models	Sleep modulates the cortisol rhythm; sleep loss can increase it, especially in the evening, with inconsistent results.	biologically consistent evidence	moderate
[1]	Crossover experimental study	Healthy young men	After partial restriction or total deprivation, evening plasma cortisol increased by 37% and 45%, respectively.	direct confirmation	moderate
[2]	Crossover experimental study	11 healthy young men	Six nights with four hours in bed increased evening cortisol and reduced glucose tolerance.	direct confirmation	moderate
[3]	Crossover experimental study	11 healthy volunteers	Two nights of fragmented sleep increased morning cortisol and reduced insulin sensitivity.	indirect confirmation	moderate
[4]	Systematic review and meta-analysis	24 human studies	The average effect of acute deprivation on cortisol was not significant in the overall analysis, but emerged in some subgroups.	discordant evidence	moderate

9. SINTESI EDITORIALE E CONCLUSIONI

CONCLUSIONS

The publication analyzed plausibly argues that sleep and circadian rhythms work together to regulate cortisol. The passage in the book regarding the increase in cortisol after prolonged wakefulness is moderately supported, especially concerning the increases observed in the evening following acute or repeated sleep loss. The available evidence also indicates consistency with reduced insulin sensitivity and poorer glucose regulation. However, it does not prove that cortisol is the sole cause of these alterations, nor that the effect occurs with identical intensity in every person. Further confirmation is needed in larger samples, with repeated measurements and comparable protocols.

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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