

# Stress and Sleep Disorder <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3538178/>

## Abstract

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The purpose of this study was to review potential, physiological, hormonal and neuronal mechanisms that may mediate the sleep changes. This paper investigates the literatures regarding the activity of the hypothalamic-pituitary-adrenal (HPA) axis, one of the main neuroendocrine stress systems during sleep in order to identify relations between stress and sleep disorder and the treatment of stress-induced insomnia. Sleep and wakefulness are regulated by the aminergic, cholinergic brainstem and hypothalamic systems. Activation of the HPA and/or the sympathetic nervous systems results in wakefulness and these hormones including corticotropin-releasing hormone (CRH), adrenocorticotrophic hormone (ACTH), cortisol or corticosterone, noradrenaline, and adrenaline, are associated with attention and arousal. Stress-related insomnia leads to a vicious circle by activating the HPA system. An awareness of the close interaction between sleep and stress systems is emerging and the hypothalamus is now recognized as a key center for sleep regulation, with hypothalamic neurotransmitter systems providing the framework for therapeutic advances. An updated understanding of these systems may allow researchers to elucidate neural mechanisms of sleep disorder and to develop effective intervention for sleep disorder.

## INTRODUCTION

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Stress is a complex condition with emotional, cognitive, and biological factors. Excessive stress causes long- and short-term disability in the various human systems, and activates the defense system of the central nervous system. The stress responses differ depending on the type of stress and the individual's physiological responses. These latter responses consist of neuro-endocrine and behavioral responses, and include the changes in the activity and immune function of the hypothalamo-pituitary-adrenal (HPA) axis.

Sleep is an important component of human homeostasis. Sleep disorders are closely associated with significant medical, psychological and social disturbances. Chronic sleep restriction is an increasing problem in many countries. Since the body's stress systems play a critical role in adapting to a continuously changing and challenging environment, it is an important question whether these systems are affected by sleep loss. The human body mobilizes defensive processes in an adaptive effort to maintain homeostasis. If these defenses fail, insomnia may occur. Short-term insomnia is caused by a change in routine such as psychiatric illness, disability, and stress [1].

In the beginning of sleep, the activity of HPA axis is suppressed continually. In the latter part of sleep, the HPA secretory activity increases so it is close to the maximum circadian rhythm immediately after waking up, and the prominent activity of the HPA axis and sympathetic nervous system influences the overall amount of rapid eye movement (REM) sleep [2]. Therefore, the rise of adrenocorticotrophic hormone (ACTH) in the morning is the decisive control factor regulating the end of sleep [3]. The fact that the beginning and end of sleep involve HPA axis activity and the close temporal relationship between the axis and sleep provides a clue to estimate the effects of the stress on sleep.

The immune system is also influential in the relationship between stress and sleep. The most important link between the immune system and sleep is established by the cytokines which act as signaling molecules of the immune system such as interleukin-1 beta (IL-1 $\beta$ ), tumor necrosis factor (TNF), and interferon. IL-1 $\beta$ , TNF, and interferon are known to participate in the regulation of sleep [4]. If IL-1 $\beta$  or TNF are injected, non-REM (NREM) sleep will increase. But, in the absence of these

substances, sleep is interrupted. IL-1 $\beta$  is also involved with the immune regulating feedback chain, which activates the HPA axis, and may be one pathway involved in the relationship between stress and sleep [5].

Typically, stress-related insomnia is transient and persists for only a few days. But, in the clinic setting the real problem is chronic insomnia, which is also called physiological insomnia. The stress-diathesis theory of the onset of chronic insomnia posits the involvement of a series of steps configured by the predisposing, precipitating, and perpetuating factors. A greater understanding is needed about the progress of insomnia caused by stress, particularly physiological insomnia.

In this study, the factors involved in sleep and alertness, their mechanisms of regulation, and the regulatory influences of the activation of HPA axis on stress-related physiological responses and changes in immune function on regulating sleep and alertness mechanisms were examined. As well, the mechanisms by which transient insomnia due to stress becomes chronically stabilized were investigated.

General Questions:

1. What is the main focus of the study?
- a) The relationship between exercise and sleep
  - b) The relationship between stress and sleep disorders

2. Which physiological systems are mentioned as playing a role in regulating sleep and stress?
- a) The digestive and respiratory systems
  - b) The hypothalamic-pituitary-adrenal (HPA) axis and the immune system

3. What is highlighted as a consequence of chronic stress in the text?
- a) Increased appetite
  - b) Long- and short-term disability in various human systems

Specific Questions:

4. What is the role of corticotropin-releasing hormone (CRH) in sleep and wakefulness?
- a) It promotes sleep
  - b) It is associated with attention and arousal

5. What is the decisive control factor regulating the end of sleep according to the text?
- a) Adrenocorticotrophic hormone (ACTH)

b) Cortisol

6. Which cytokines are mentioned as influencing the regulation of sleep?
- a) Interleukin-6 and interferon-gamma
  - b) Interleukin-1 beta (IL-1 $\beta$ ) and tumor necrosis factor (TNF)

7. What term is used to describe chronic insomnia caused by stress?
- a) Psychiatric insomnia
  - b) Physiological insomnia

8. According to the stress-diathesis theory, what factors are involved in the onset of chronic insomnia?
- a) Predisposing, precipitating, and perpetuating factors
  - b) Hormonal, genetic, and environmental factors

9. What is identified as the main problem in the clinic setting regarding insomnia?
- a) Transient insomnia
  - b) Chronic insomnia

10. What is the primary focus of the study's investigation?
- a) The mechanisms of REM sleep
  - b) The regulatory influences of the HPA axis on stress-related physiological responses and changes in immune function on regulating sleep and alertness mechanisms