SLEEP, IMMUNITY AND VACCINE EFFICACY IN DISEASE PREVENTION

Nguyen Duy Thai[1*], Tran Hong Tram[1], Doan Huu Thien[1], Vu Thi Lan Anh[2], Do Thi Huong[2], Dang Anh Ngoc[2], Vuong Thi Mai Linh[2], Nguyen Thi Thu Hien[2], Doan Huu Xuyen[2]

[1] National Institute for Control of Vaccines and Biologicals, Ministry of Helth

[2]Vietnam University of Traditional Medicine

Received 01 April 2024
Accepted 30 August 2024

Abstract: Sleep is crucial for health and strengthens the immune system, aiding the body in fighting diseases. Research indicates that adequate and quality sleep enhances vaccine efficacy by boosting immune responses, increasing antibody production, and preventing the spread of pathogens. To understand the role and mechanism of sleep in vaccine effectiveness, we searched and screened over 2,000 open-access articles on PubMed and Scopus using relevant keywords following the PRISMA guidelines. Results showed that 7 or more hours of sleep each night increase antibody titers and improve vaccine efficacy and immune memory. Thus, it is essential to focus on enhancing sleep quality and provide appropriate recommendations in vaccination strategies to help care for, protect health, and control epidemics in the community.

Keywords: *Sleep, immunity, vaccines, pathogens, pandemic.*

[*] Corresponding author
E-mail address: thainguyenduy@hotmail.com
https://doi.org/10.56086/jcvb.v4i3.161

1. Introduction

Sleep is an indispensable part of life, playing a vital role in maintaining health, homeostatic balance, immune system function, and overall body performance [1]. Therefore, sleep significantly impacts immune function and vaccine efficacy [2]. Sleep deprivation not only diminishes the body's ability to respond to vaccines but also increases the risk of contracting severe diseases. Studies have shown a link between sleep disorders and poor immune responses. Specifically, individuals who do not get enough sleep produce fewer antibodies after vaccination. For example, a group of young, healthy individuals restricted to only 4 hours of sleep per night for 6 nights before receiving the influenza vaccine, followed by recovery with 12 hours of sleep each night for 7 nights, produced fewer antibodies compared to those who had regular sleep duration 10 days after vaccination [3, 4].

In another study, individuals who had sufficient sleep after receiving the hepatitis A vaccine had an antibody response twice as strong as those who were not allowed to sleep for 36 hours post-vaccination [5]. This might be due to sleep stimulating the release of immune-boosting hormones and reducing stress hormones. Notably, participants in this study had never contracted hepatitis A and had very low antibody levels before vaccination, indicating that sleep can modulate the initial immune response. The study also showed a marked difference in adaptive immunity that persisted after 1 year, demonstrating that sleep can enhance immune memory. In adults, sleep duration also affects vaccine efficacy. Research on a group of individuals with no prior hepatitis B antibodies found that those who slept less, especially two nights before and after receiving the hepatitis B vaccine, had lower antibody levels after 1 and 4 months compared to the group that slept sufficiently. Similar results were found after the second and third doses [6]. In reality, each additional hour of sleep can increase antibody concentration by 56%. This suggests that sleep deprivation may reduce antibody responses, at least in the early stages, and prolong cellular immunity deficits across various vaccines. Therefore, maintaining adequate sleep can improve immune responses and vaccine efficacy [4,7].

The COVID-19 pandemic has profoundly affected the sleep of many people, causing anxiety, stress, and pressure. Social restriction measures, such as quarantine and social distancing, also contributed to lifestyle disruptions and sleep pattern changes [8-10]. Many studies have shown that decreased sleep quality, insomnia, and other sleep disorders have increased due to declining mental health, reduced physical activity, and social isolation [11,12]. Meanwhile, vaccination is the most effective measure to prevent the spread of the SARS-CoV-2 virus. Although initial reports indicated that vaccines like Pfizer-BioNTech and Moderna were about 95% effective in clinical trials, real-world efficacy and vaccine protection were lower due to various factors [13].

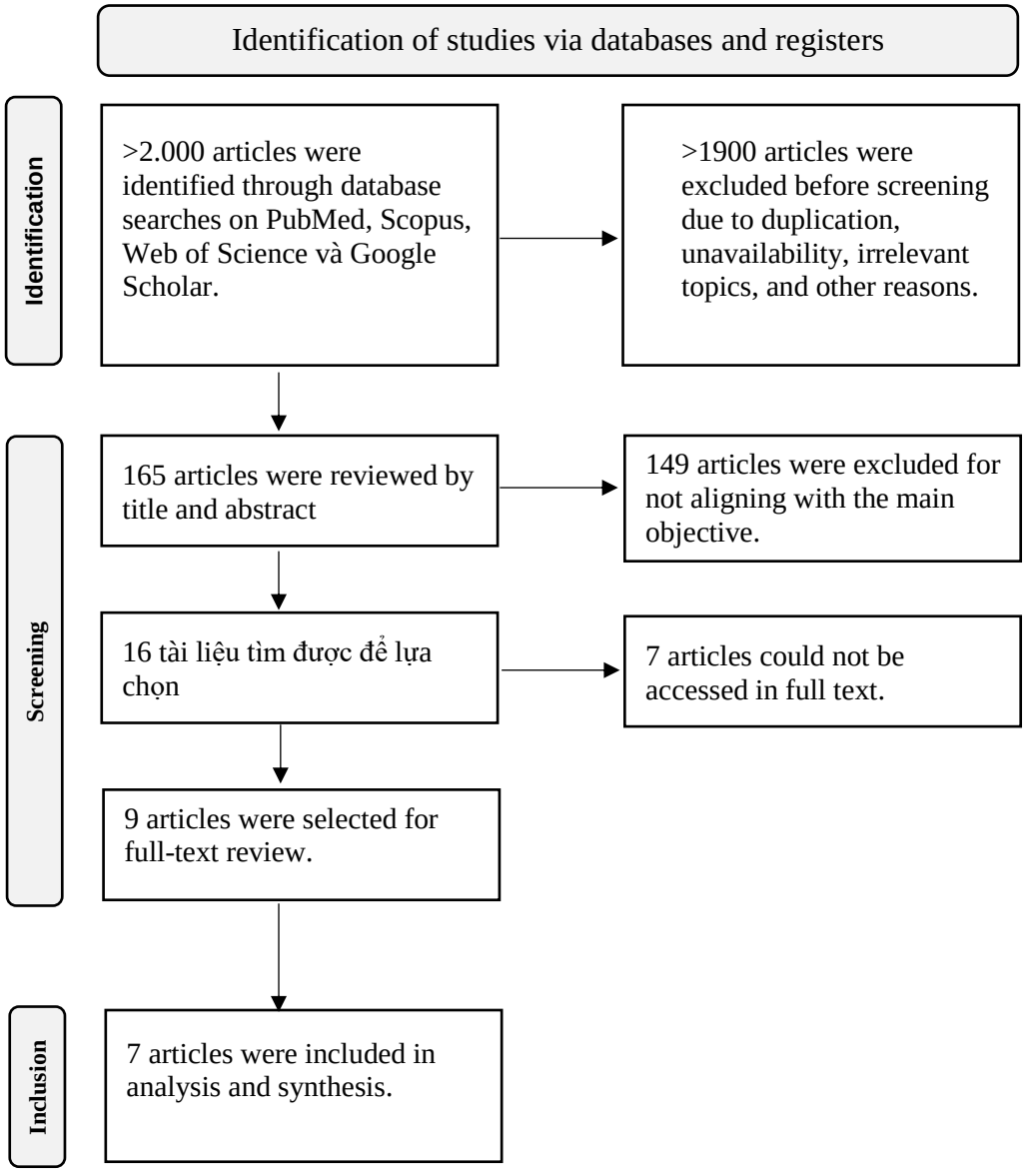
No specific research has yet determined the impact of sleep on the effectiveness of the COVID-19 vaccine. However, data from other vaccines have

shown that sleep duration and quality can influence their efficacy. This study aims to better understand the relationship between sleep and vaccine efficacy and to find measures to mitigate negative impacts on health during the COVID-19 pandemic.

2. Methods

We searched for open-access articles in PubMed and Scopus databases using the keywords: (sleep OR insomnia OR sleep deprivation OR sleep disorders) AND (immunity OR vaccination efficacy OR vaccine effectiveness OR COVID-19). The search was limited to English publications up to December 31, 2023. From over 2,000 articles found, after screening based on eligibility criteria, we selected 7 articles suitable for analysis in this study. The evaluation process followed the PRISMA guidelines (Figure 1).

Figure 1. Diagram of research material selection process according to PRISMA



3. Results

3.1. Sleep and the Immune System

Sleep plays an important role in daily life, profoundly affecting health and body functions. The ability to maintain wakefulness or long-term sleep depends on the interaction between the endocrine biological system and the sleep control system [14, 15]. Sleep and wake cycles are synchronized with the 24-hour light-dark cycle of the environment, regulated by the circadian rhythm system, including the "Master clock" in the hypothalamus and peripheral clocks in organs and tissues [16]. Circadian rhythms also appear in immune system cells such as macrophages, monocytes, neutrophils, and NK cells [17]. Sleep and circadian rhythms play an essential role in regulating the immune system, including both innate and adaptive immunity [18]. The immune system can remember and respond more quickly when re-encountering previously exposed pathogens through immune memory, including antibody production after vaccination and the activity of T lymphocytes, B lymphocytes, and circulating antibodies in the body.

The immune system combats infections and repairs cellular damage through inflammatory responses based on chemical signals called cytokines [18]. Cytokines are proteins produced by immune cells that promote intra- and extracellular immune responses [19]. Some important cytokines related to sleep and innate immunity include interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) [20]. IL-6 is an inflammatory cytokine that reduces anabolic pathways and increases catabolic pathways, leading to increased energy expenditure and decreased weight gain. TNF-α is also an inflammatory cytokine that functions in lipid breakdown, adipose tissue regulation, immune modulation, apoptosis, proliferation, and pathological responses [21].

Sleep helps maintain the regular expression of immune cells such as monocytes, macrophages, and dendritic cells over a 24-hour period. However, sleep disorders can alter the expression of these cells. For example, IL-6, an inflammatory cytokine, typically peaks at 7 p.m. and 5 a.m. Nighttime sleep deprivation can delay or reduce IL-6 secretion, proportional to sleep loss duration, as well as increase monocyte count and bacterial challenge response during sleep [22]. Although short-term sleep deprivation does not significantly change immune cell counts, chronic sleep loss can alter immune cell phenotype distribution. Specifically, CD3+, CD4+, and CD8+ cell numbers can decrease significantly due to prolonged sleep deprivation [27].

Studies show that sleep deprivation and short sleep habits lead to higher pro-inflammatory cytokine secretion. Groups sleeping less than 6 hours each night exhibit diminished T lymphocyte activity, lower NK cell levels, shorter T cell telomere lengths, and increased inflammatory markers like C-reactive protein and IL-6 [23]. Additionally, those sleeping less than 5 hours have a higher risk of upper respiratory infections and acute bronchitis compared to those sleeping 7 to 8 hours each night [24]. Another study on chronic fatigue syndrome

patients found those with the poorest sleep quality had higher fatigue levels, more interference with daily activities, and increased interleukin levels, such as IL-1β, TNF-α, and IL-6 [25].

Moreover, higher circulating immune cell numbers, such as neutrophils and B cells, indicate that sleep plays a role in leukocyte trafficking similar to circadian clocks [26]. Inflammatory responses are crucial in protecting the body from pathogens, but chronic imbalance during inflammation can negatively impact the immune system. Continuous pro-inflammatory states can impair immune tolerance and normal immune function, making the body vulnerable to pathogens like viruses.

Sleep deprivation affects immune parameters such as leukocyte counts, cytokine levels, complement factors in blood, and cellular toxicity. Studies show that adequate sleep reduces leukocyte numbers and distribution compared to complete or partial sleep deprivation [27]. Specifically, a reduction in the total number of lymphocytes, monocytes, and NK cells during adequate sleep was observed [28]. Leukocytes are immune cells that can move throughout the body via the blood and lymphatic system, decreasing in number in the blood when redistributed to lymph nodes, organs, and tissues during sleep, reducing viral infection risk. Sleep-deprived individuals have fewer leukocytes in lymph nodes, reducing their ability to mount a rapid immune response, making them more susceptible to infectious diseases. Studies in mice have shown that sleep deprivation and REM sleep deprivation increase levels of inflammatory cytokines such as IL-1α, IL-1β, IL-6, IL-10, TNF, and IL-17A. Sleep deprivation is also associated with elevated inflammatory response markers such as C-reactive protein (CRP) and IL-6 [29]. When faced with an inflammatory challenge, the number of circulating monocytes increases, as does the number of cytokines produced per cell, leading to a significant increase in cytokines such as IL-6 and TNF-alpha [30]. This suggests that sleep deprivation alters the immune system, affecting cytokine production, leading to chronic imbalance in immune function, inflammation, and increased susceptibility to viral infections [31]. The activity and proliferation of immune cells are also affected by sleep deprivation. Following sleep deprivation, NK cell activity decreases in the morning but increases in the evening after two days without sleep [32]. These differences may be due to the time of day of activity measurement (morning and evening), or NK cell function may diminish if sleep is deprived; however, if sleep deprivation persists, NK cell activity returns to normal to adapt to the circumstances rather than further diminishing function. When considering proliferation, particularly lymphocyte cells, sleep has a similarly complex effect. Lymphocyte proliferation rates decrease after sleep deprivation but increase again after several nights of recovery sleep [30]. It suggests that compensatory mechanisms occur after a few nights of sleep deprivation for proliferation processes.

3.2 Sleep and Vaccine Efficacy

The impact of sleep on immune function, particularly the body's responsiveness when exposed to viruses, has been extensively studied. However, studies often focus on individual immune indicators. In reality, effective immune responses are far more complex, requiring the interaction of multiple immune cell types and mediators of both innate and adaptive immunity. Therefore, relevant findings must be studied in the context of the entire immune response. Vaccination is an excellent experimental model for this study because it simulates infection and can be performed on healthy individuals at any time.

Vaccine-induced immunity is based on the complex interaction between innate immunity, humoral immunity, and cell-mediated immunity. Vaccines are one of the most cost-effective medical interventions, estimated to save approximately 25 million lives annually. Immune responses to vaccination vary among individuals in terms of quantity and quality [33]. Vaccines ensure immune memory, and sleep is thought to support this process, making vaccination more effective. Understanding the mechanism of memory formation can help understand the role of sleep in immune memory. The formation of immune memory can be understood through three stages, similar to the central nervous system (CNS). The first is the encoding stage, where antigen-presenting cells (APCs) recognize foreign antigens and initiate an immune response. The next stage is consolidation, where information from short-term storage is transferred to long-term storage through T and B cell memory in secondary lymphoid tissues. In secondary lymphoid tissues, information is transmitted from APCs to T and B cells, which, when activated, produce effector and memory cells and then produce antibodies. Finally, the recall stage occurs when memory T and B cells are reactivated when encountering the antigen. Understanding this mechanism clarifies sleep's role in enhancing immune memory and vaccine efficacy.

Sleep appears to support immune memory consolidation by reducing the number of circulating antigen-presenting cells (APCs) and T lymphocytes, redirecting them to lymph nodes. This increases the interaction between APCs and T cells, facilitating more effective information transfer from APCs to T cells. Sleep also promotes the production of pro-inflammatory cytokines, further supporting this interaction. Regarding its supportive role in immune formation, slow-wave sleep (SWS) or deep sleep seems particularly suitable for this process [34]. Indeed, SWS reduces the number of APC precursors and T cells in the blood, facilitating their transport to lymph nodes and increasing interaction opportunities [28]. SWS also increases IL-12 and IL-17 concentrations and reduces cortisol levels, creating a pro-inflammatory environment that promotes immune memory establishment [23]. Existing literature supports that SWS promotes the migration and communication between T cells and APCs in lymph nodes through immune-supportive hormonal groups, improving adaptive immune

responses and ensuring more robust immune memory [23].

Sleep and immune responses have a bidirectional relationship. Nighttime sleep creates a supportive environment for activating adaptive cellular immune responses by regulating IL-10 and IL-12 activities [35]. Sleep acts as a natural adjuvant by promoting the formation of immune synapses between antigen-presenting cells and CD4+ T cells, thereby activating cellular and humoral immunity [36]. When the immune system is activated, inflammatory cytokines such as IL-1β and TNF-α cross the blood-brain barrier and induce sleep. While sleeping, growth hormone (GH) and insulin-like growth factor-1 (IGF-1) levels increase along with prolactin levels, while cortisol secretion is inhibited. This creates a favorable environment for activating helper T cells, cytotoxic T cells, and B cells. This leads to the production of virus-specific antibodies by B cells and CD4+ and CD8+ T cells, helping form memory T cells to maintain long-term immunity against pathogens.

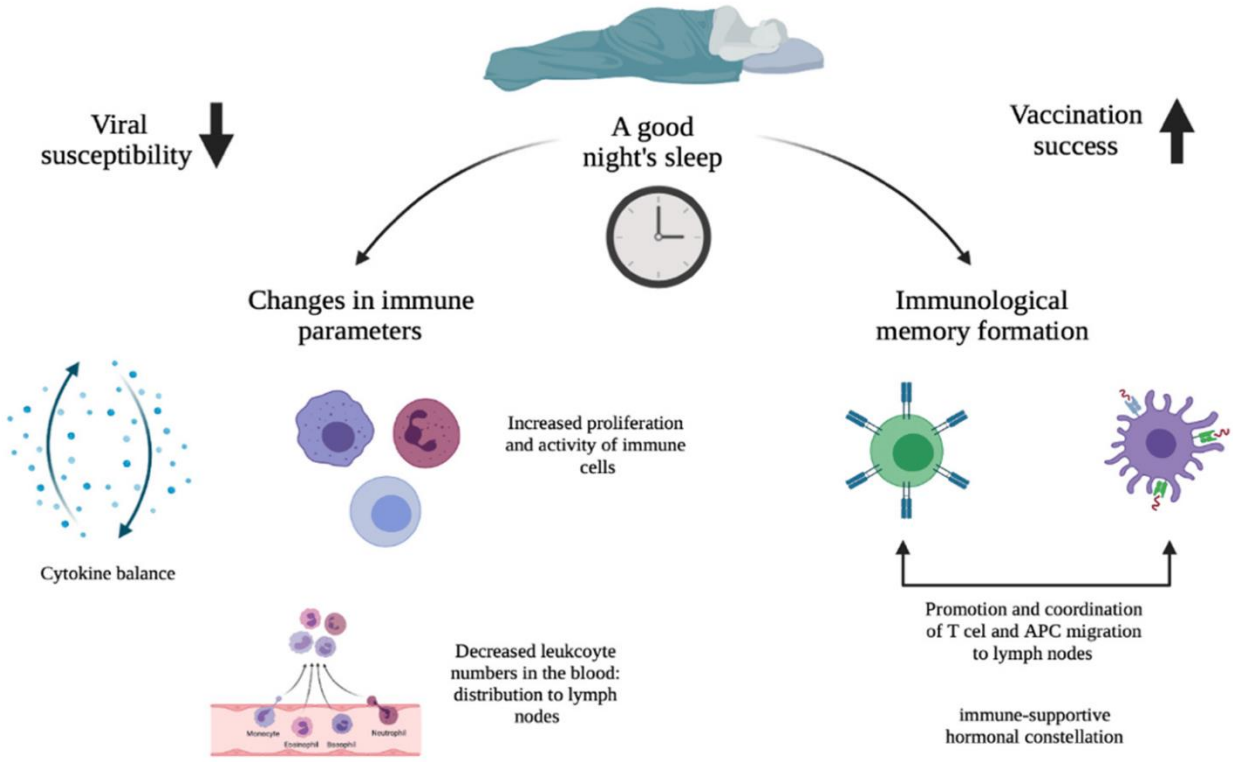


Figure 2. Diagram of the Relationship Between Sleep and Vaccination Efficacy through the Immune System [37].

(*Quality sleep leads to optimal day-night balance, immunity, cytokine production, and virus sensitivity, thereby improving vaccination efficacy through a better immune response to vaccine antigens)*

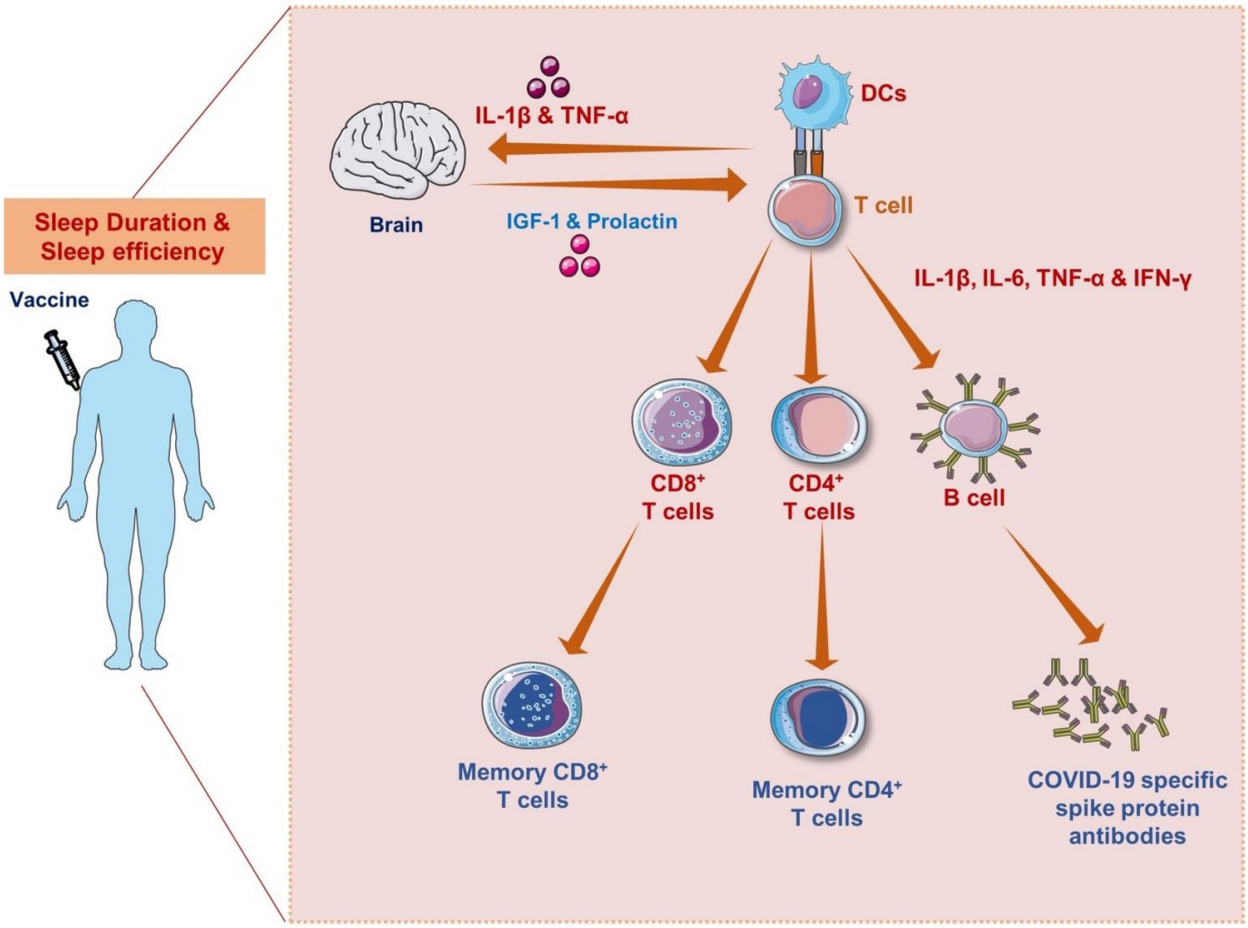


Figure 3. Link Between Sleep Deprivation and Immune Response After COVID-19 Vaccination [38].

(Sleep acts as an adjuvant, promoting GH prolactin secretion and inhibiting cortisol to activate naïve T cells. This enhances IL-6, IL-8, IFN-γ, IL-1β, and TNF-α release and promotes CD4+ T cell activation via cell-mediated and humoral immunity activation).

4. Discussion

The impact of sleep on the immune system and vaccination efficacy are two extensively studied research topics. Sleep and immune activity are intricately linked and influence each other. When the body is susceptible to viral infections, disrupted sleep can alter cytokine production, causing imbalances in the immune system and facilitating a pro-inflammatory state. This pro-inflammatory environment increases susceptibility to bacteria and viruses, weakening the immune system. In vaccination, both sleep duration and time of day affect the intensity of antibody responses post-vaccination. The immune response from vaccination plays a crucial role in creating immune memory, and sleep supports this process. Numerous studies have shown the relationship between sleep and immune response efficacy post-vaccination, indicating that adequate sleep can enhance vaccination efficacy.

The first study on the impact of sleep on vaccination and immune response was conducted with the influenza vaccine. Participants were divided into two groups: one sleeping 4 hours each night and the

other sleeping 7-8 hours each night for 4 days before and 2 days after vaccination. After ten days, the results showed that the well-slept group had antibody levels twice as high as the restricted sleep group [4]. Another study on the influenza vaccine confirmed similar results. Participants recorded sleep diaries 13 days before and after receiving the flu vaccine. The results indicated that less sleep, especially in the two nights before vaccination, led to lower antibody levels after 1 and 4 months [39]. A study on the impact of 24-hour sleep-wake cycles with the H1N1 vaccine in healthy individuals found that sleep-deprived men had lower antibody levels 5 days post-vaccination compared to those with adequate sleep. This indicates that sleep has an early impact on immune responses [35]. Another study by Taylor and colleagues also demonstrated that sleep-deprived individuals had lower serum influenza antibody concentrations after one year, suggesting that sleep deprivation may be a risk factor for reduced influenza vaccine response. These results align with reports of associations between short sleep and decreased antibody responses after flu vaccination [40].

Studies on the impact of sleep on immune memory formation have examined vaccines against hepatitis. Lange and colleagues studied healthy men vaccinated against hepatitis A three times at weeks 0, 8, and 16. They were then divided into sleep and wake groups for follow-up on the night after vaccination. Sleep was recorded using polysomnography, and hormone concentrations were measured overnight through blood sampling (via an arm catheter). T and B cell (antibody) responses were monitored up to one year post-vaccination. The results showed that antigen-specific T cells doubled when participants slept 7-8 hours on the night after vaccination compared to the awake group. This indicates that sleep has an early impact on immune responses, possibly due to the interaction between APCs and T cells in lymphoid tissues. Increased T cell numbers were accompanied by a higher proportion of cytokine-producing inflammatory cells, supporting the cellular aspects of adaptive immune responses. Additionally, SWS stimulates the release of immune-supportive hormones such as growth hormone and prolactin while reducing the release of immune-suppressive hormone cortisol. The interaction between APCs and T cells and the response to vaccination are influenced by growth hormone and prolactin [7]. Another study by Lange and colleagues also showed that the well-slept group after hepatitis A vaccination had nearly double the antibody titers compared to the awake group, a finding noted 4 weeks post-vaccination. However, no short-term effects were found in this study [5].

Both cross-sectional and experimental studies indicate that disrupted sleep impairs antibody responses after vaccination. Shorter sleep duration leads to diminished cell-mediated immunity with various vaccines. During the COVID-19 pandemic, many people's sleep was disrupted, and most studies reported people sleeping less or more than before the pandemic [41]. In China, during the

COVID-19 outbreak, data showed that over 20% of the population met the criteria for clinical insomnia and typically stayed awake for over 1 hour each night. Individuals at high risk of SARS-CoV-2, including healthcare workers, experienced worsened insomnia, negatively affecting immunity and vaccination efficacy [42]. To ensure higher vaccination success rates, especially with current vaccination strategies, individuals should sleep at least 7 hours each night. Sleep and biologically-based interventions can optimize sleep and regulate circadian rhythms before vaccination.

Overall, current studies in humans provide compelling evidence that good sleep will help enhance the efficacy of vaccination strategies. However, more in-depth research is needed to propose specific solutions to raise awareness among the population and the community about the importance of sleep for vaccination efficacy.

This comprehensive evaluation study has limitations due to the research scope being limited to a few databases and languages. Furthermore, insufficient quality assessments and heterogeneity in the analysis methods of studies may affect the process of comparing, synthesizing results, and drawing conclusions.

5. Conclusionn

Based on published data on changes in immune response, vaccination efficacy, and infection risk, the critical role of sleep as an essential factor in determining vaccine efficacy has been demonstrated. Sleeping 7 hours or more each night positively impacts antibody responses post-vaccination by increasing antibody titers and significantly improving vaccination efficacy and immune memory formation. Therefore, recommendations for improving sleep quality should be emphasized in vaccination strategies.

References

[1] Krueger JM, Frank MG, Wisor JP, Roy S. Sleep function: Toward elucidating an enigma. Sleep medicine reviews. 2016;28:46-54.

[2] Hirshkowitz M, Whiton K, Albert SM, Alessi C, Bruni O, DonCarlos L, et al. National Sleep Foundation's updated sleep duration recommendations: final report. Sleep Health. 2015;1(4):233-43.

[3] Burns VE, Drayson M, Ring C, Carroll D. Perceived stress and psychological well-being are associated with antibody status after meningitis C conjugate vaccination. Psychosomatic medicine. 2002;64(6):963-70.

[4] Spiegel K, Sheridan JF, Van Cauter E. Effect of sleep deprivation on response to immunizaton. JAMA. 2002;288(12):1471-2.

[5] Lange T, Perras B, Fehm HL, Born J. Sleep Enhances the Human Antibody Response to Hepatitis A Vaccination. Psychosomatic Medicine. 2003;65(5):831-5.

[6] Prather AA, Hall M, Fury JM, Ross DC, Muldoon MF, Cohen S, et al. Sleep and antibody response to hepatitis B vaccination. Sleep. 2012;35(8):1063-9.

[7] Lange T, Dimitrov S, Bollinger T, Diekelmann S, Born J. Sleep after

vaccination boosts immunological memory. The Journal of Immunology. 2011;187(1):283-90.

[8] Zachary Z, Brianna F, Brianna L, Garrett P, Jade W, Alyssa D, et al. Self-quarantine and weight gain related risk factors during the COVID-19 pandemic. Obesity research & clinical practice. 2020;14(3):210-6.

[9] Casagrande M, Favieri F, Tambelli R, Forte G. The enemy who sealed the world: effects quarantine due to the COVID-19 on sleep quality, anxiety, and psychological distress in the Italian population. Sleep medicine. 2020;75:12-20.

[10] Hartley S, Des Francs CC, Aussert F, Martinot C, Dagneaux S, Londe V, et al. Les effets de confinement SARS-CoV-2 sur le sommeil: enquête en ligne au cours de la quatrième semaine de confinement. L'Encéphale. 2020;46(3):S53-S9.

[11] Gupta R, Grover S, Basu A, Krishnan V, Tripathi A, Subramanyam A, et al. Changes in sleep pattern and sleep quality during COVID-19 lockdown. Indian journal of psychiatry. 2020;62(4):370-8.

[12] Datta K, Tripathi M. Sleep and COVID-19. Neurology India. 2021;69(1):26-31.

[13] Mahase E. Covid-19: Moderna vaccine is nearly 95% effective, trial involving high risk and elderly people shows. BMJ: British Medical Journal (Online). 2020;371.

[14] Zielinski MR, McKenna JT, McCarley RW. Functions and mechanisms of sleep. AIMS Neurosci. 2016;3(1):67.

[15] Borbély AA. A two process model of sleep regulation. Hum neurobiol. 1982;1(3):195-204.

[16] Ramkisoensing A, Meijer JH. Synchronization of biological clock neurons by light and peripheral feedback systems promotes circadian rhythms and health. Frontiers in neurology. 2015;6:138217.

[17] Comas M, Gordon CJ, Oliver BG, Stow NW, King G, Sharma P, et al. A circadian based inflammatory response–implications for respiratory disease and treatment. Sleep Science and Practice. 2017;1:1-19.

[18] Libby P, Nahrendorf M, Swirski FK. Leukocytes link local and systemic inflammation in ischemic cardiovascular disease: an expanded “cardiovascular continuum”. Journal of the American College of Cardiology. 2016;67(9):1091-103.

[19] Chokroverty S, Ferini-Strambi L. Oxford textbook of sleep disorders: Oxford University Press; 2017.

[20] Irwin MR. Why sleep is important for health: a psychoneuroimmunology perspective. Annu Rev Psychol. 2015;66:143-72.

[21] Holbrook J, Lara-Reyna S, Jarosz-Griffiths H, McDermott MF. Tumour

necrosis factor signalling in health and disease. F1000Res. 2019;8.

[22] Redwine L, Hauger RL, Gillin JC, Irwin M. Effects of sleep and sleep deprivation on interleukin-6, growth hormone, cortisol, and melatonin levels in humans. The Journal of Clinical Endocrinology & Metabolism. 2000;85(10):3597-603.

[23] Besedovsky L, Lange T, Haack M. The sleep-immune crosstalk in health and disease. Physiological reviews. 2019.

[24] Prather AA, Leung CW. Association of insufficient sleep with respiratory infection among adults in the United States. JAMA internal medicine. 2016;176(6):850-2.

[25] Milrad SF, Hall DL, Jutagir DR, Lattie EG, Ironson GH, Wohlgemuth W, et al. Poor sleep quality is associated with greater circulating pro-inflammatory cytokines and severity and frequency of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) symptoms in women. Journal of neuroimmunology. 2017;303:43-50.

[26] Haspel JA, Anafi R, Brown MK, Cermakian N, Depner C, Desplats P, et al. Perfect timing: circadian rhythms, sleep, and immunity—an NIH workshop summary. JCI insight. 2020;5(1).

[27] Faraut B, Boudjeltia KZ, Dyzma M, Rousseau A, David E, Stenuit P, et al. Benefits of napping and an extended duration of recovery sleep on alertness and immune cells after acute sleep restriction. Brain, behavior, and immunity. 2011;25(1):16-24.

[28] Born J, Lange T, Hansen K, Mölle M, Fehm H-L. Effects of sleep and circadian rhythm on human circulating immune cells. Journal of immunology (Baltimore, Md: 1950). 1997;158(9):4454-64.

[29] Meier-Ewert HK, Ridker PM, Rifai N, Regan MM, Price NJ, Dinges DF, et al. Effect of sleep loss on C-reactive protein, an inflammatory marker of cardiovascular risk. Journal of the American College of Cardiology. 2004;43(4):678-83.

[30] Irwin MR, Wang M, Campomayor CO, Collado-Hidalgo A, Cole S. Sleep deprivation and activation of morning levels of cellular and genomic markers of inflammation. Archives of internal medicine. 2006;166(16):1756-62.

[31] Ibarra-Coronado EG, Pantaleón-Martínez AM, Velazquéz-Moctezuma J, Prospéro-García O, Méndez-Díaz M, Pérez-Tapia M, et al. The bidirectional relationship between sleep and immunity against infections. Journal of immunology research. 2015;2015.

[32] Dinges D, Douglas S, Zaugg L, Campbell D, McMann J, Whitehouse W, et al. Leukocytosis and natural killer cell function parallel neurobehavioral fatigue induced by 64 hours of sleep deprivation.

The Journal of clinical investigation. 1994;93(5):1930-9.

[33] Zimmermann P, Curtis N. Factors that influence the immune response to vaccination. Clinical microbiology reviews. 2019;32(2):10.1128/cmr. 00084-18.

[34] Besedovsky L, Ngo H-VV, Dimitrov S, Gassenmaier C, Lehmann R, Born J. Auditory closed-loop stimulation of EEG slow oscillations strengthens sleep and signs of its immune-supportive function. Nature communications. 2017;8(1):1984.

[35] Benedict C, Brytting M, Markström A, Broman J-E, Schiöth HB. Acute sleep deprivation has no lasting effects on the human antibody titer response following a novel influenza A H1N1 vi rút vaccination. BMC immunology. 2012;13:1-5.

[36] Benedict C, Cedernaes J. Could a good night's sleep improve COVID-19 vaccine efficacy? The Lancet Respiratory Medicine. 2021;9(5):447-8.

[37] Schmitz NC, van der Werf YD, Lammers-van der Holst HM. The importance of sleep and circadian rhythms for vaccination success and susceptibility to viral infections. Clocks & sleep. 2022;4(1):66-79.

[38] Akhtar N, Srivastava RK, Shrivastava D. How Losing Sleep Following Vaccination May Weaken the Response to SARS-CoV Vaccines. Sleep and Vigilance. 2022;6(1):249-51.

[39] Prather AA, Pressman SD, Miller GE, Cohen S. Temporal links between self-reported sleep and antibody responses to the influenza vaccine. International journal of behavioral medicine. 2021;28:151-8.

[40] Taylor DJ, Kelly K, Kohut ML, Song K-S. Is insomnia a risk factor for decreased influenza vaccine response? Behavioral sleep medicine. 2017;15(4):270-87.

[41] Batool-Anwar S, Robbins R, Ali SH, Capasso A, Foreman J, Jones AM, et al. Examining changes in sleep duration associated with the onset of the COVID-19 pandemic: Who is sleeping and who is not? Behavioral Medicine. 2023;49(2):162-71.

[42] Kim H, Hegde S, LaFiura C, Raghavan M, Luong E, Cheng S, et al. COVID-19 illness in relation to sleep and burnout. BMJ Nutrition, Prevention & Health. 2021;4(1):132.