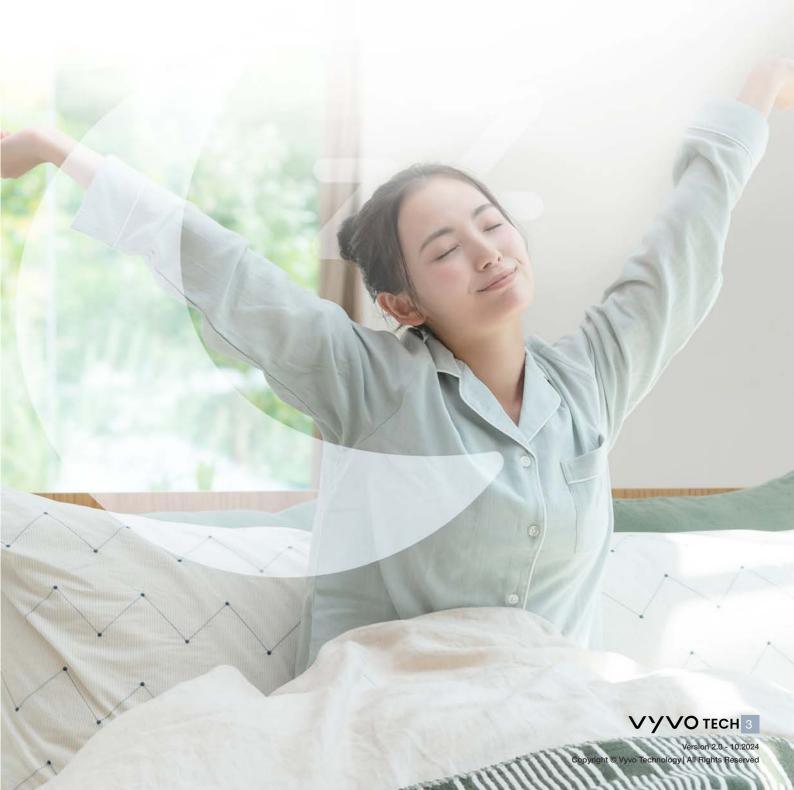


Abstract	3
Sleep Patterns	4
The Importance	
of REM Sleep	5
Sleep Quality and Health	6
Sleep Monitoring via Photoplethysmography	6 - 7 - 8
Sleep Monitoring with Vyvo Technology Wearables	9
Legal Disclaimer	8
Useful Terms	9
References	10 - 11

#### **Abstract**

High-quality sleep is important in maintaining health, as this "down time" is necessary for the body to restore and repair bodily systems. Short and poor-quality sleep have been directly linked to a series of chronic health problems, including weight gain and obesity, insulin resistance, hypertension, depression, adverse cardiovascular consequences, weakened immune response, and more. Among all stages of sleep, rapid eye movement (REM) sleep is the key factor in determining sleep quality. The most effective traditional method of sleep monitoring is spectral analysis of the sleep electroencephalogram (EEG), but there is a strong relationship between EEG and the cardiac autocorrelation coefficient of RR intervals (rRR). RR intervals can be measured by photoplethysmography (PPG), which is widely used in wearable devices, such as those produced by Vyvo Technology, which are suitable for use during sleep.



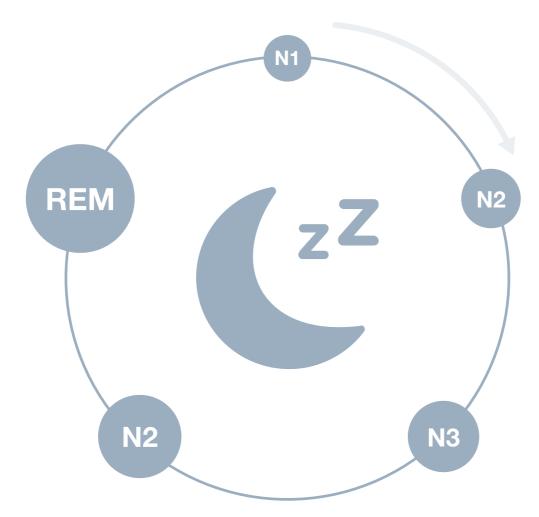
# **Sleep Patterns**

Sleep is a naturally recurring state that serves several functions, including restoration of bodily systems and memory processing. It is divided into two very distinct types, non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep. Non-REM or deep sleep, which occurs first, is characterized by reduced body temperature and heart rate, and less energy use by the brain. REM sleep, known as the dream state, represents a smaller percentage of overall sleep. It involves fast brain waves, eye movements, and relaxed muscle tone.<sup>1</sup>



The American Academy of Sleep Medicine further divides NREM sleep into three stages, N1, N2, and N3 (the deepest level of sleep). A sleep cycle of alternate NREM and REM sleep typically lasts 90 minutes, with four to six such cycles every night.

A sleep cycle "normally proceeds in the order: N1  $\rightarrow$  N2  $\rightarrow$  N3  $\rightarrow$  N2  $\rightarrow$  REM. REM sleep occurs as a person returns to stage 2 or 1 from a deep sleep. There is a greater amount of deep sleep (stage N3) earlier in the night, while the proportion of REM sleep increases in the two cycles just before natural awakening."<sup>2</sup>



## The Importance of REM Sleep

While the general populace will not be familiar with N1, N2, and N3, most will have heard of REM sleep. In this stage, the brain is highly active, the eyeballs will move quickly back and forth, and it's easy to achieve a dream state, including vivid dreams. In addition to the eye movement that gives this sleep stage its name,

REM sleep is ... characterized (and hence differentiated from wake and non-REM sleep) by other defining physiologic and behavioral features, including a reduced amplitude and faster frequency cortical electroencephalogram (EEG) that is reminiscent of waking, high-amplitude theta waves in the hippocampal EEG, active suppression of skeletal muscle activity, intermittent muscle twitches, autonomic and respiratory activation, fluctuations in brain/body temperature, and an elevated arousal threshold.

Functionally, REM sleep has been shown to play an important role in mood regulation, learning, memory, and stress management.<sup>4,5</sup> Further research points to additional benefits from REM sleep, including facilitating cortical plasticity<sup>6</sup>, restoration of aminergic cell/receptor function<sup>7</sup>, and heightening general creativity.<sup>8</sup> Research also shows that REM sleep is "regulated by sensitive homeostatic mechanisms."<sup>9</sup>

The amount of REM sleep experienced during sleep depends on various factors, such as age. For example, the REM sleep of infants accounts for 50% of the total sleep, while for adults it is only about 20%.<sup>10, 11</sup>

To maximize REM sleep, individuals should keep a regular routine, focused on early bedtimes and early wake times, and reducing mental stress. Avoiding caffeine, alcohol, cigarettes, and other chemicals that interfere with REM sleep is critical.



## Sleep Quality and Health

Short and poor-quality sleep have been directly linked to a series of chronic health problems, including weight gain and obesity, insulin resistance, hypertension, depression, adverse cardiovascular consequences, weakened immune response, and more.<sup>12, 13</sup> Research shows that excessive sleep can contribute to health concerns as well, with one study recommending that the optimal amount for adults is seven to eight hours nightly.<sup>14</sup>

Numerous factors can contribute to lower quality sleep, including diet, use of caffeine and alcohol, poor sleep environments, and physiological concerns, such as obstructive sleep apnea (OSA) or restless legs syndrome (RLS). OSA is a major form of sleep-disordered breathing (SDB), with a potential prevalence of up to 38% in the general population. It increases the risk of cardiovascular disease and causes hypoxemia, hypercapnia, nocturia, sleep fragmentation, morning headaches, and excessive daytime sleepiness.

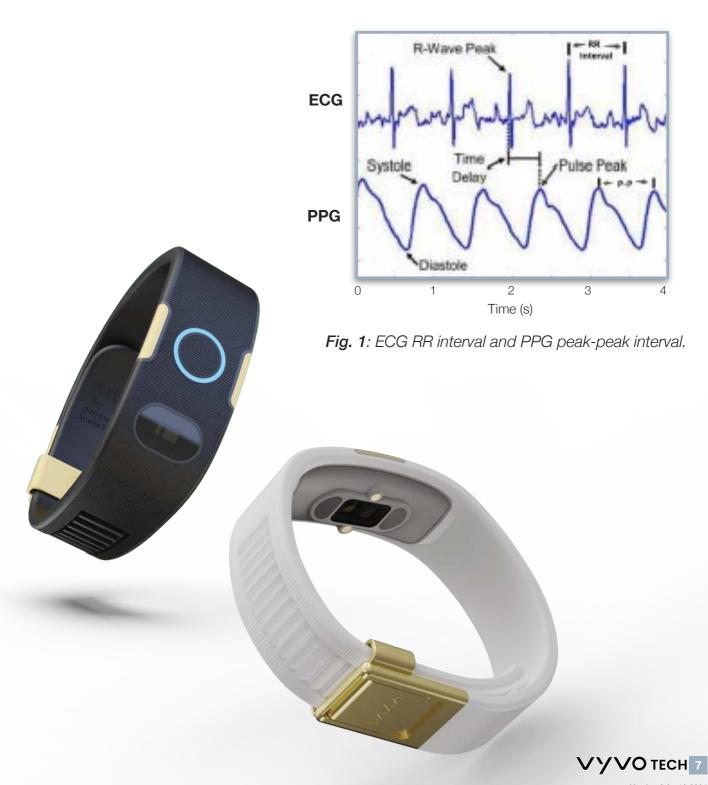
#### Sleep Monitoring via Photoplethysmography

Spectral analysis of the sleep electroencephalogram (EEG) is a traditional useful tool for quantitative and precise analysis and description of the sleep processes.<sup>17</sup> The drawback with EEG is that, in its typical format, it involves numerous electrodes placed on the head, making it highly unsuitable for daily use by consumers.



However, a useful proxy is the strong relationship between EEG and the cardiac autocorrelation coefficient of RR intervals (rRR). Otzenberger et al found "beat to beat heart rate variability and EEG activity are closely linked during sleep in normal man." This correlation is ultimately unsurprising as both REM and rRR are highly determined by the activity of the vagus nervous system.

Electrocardiogram (ECG) RR intervals can be measured with high accuracy using photoplethysmography (PPG) peak-peak intervals (see Fig. 1). Because PPG is widely and maturely used in wearable devices, these can be used to accurately monitor sleep. Fig. 2 displays the relationship between rRR and EEG, and Fig. 3 displays the relationship between rRR and REM.





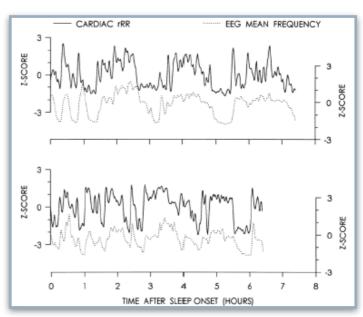


Fig. 2: Concomitant profiles of minute EEG mean frequency and of interbeat autocorrelation coefficient (rRR) after z-score transformation in two representative subjects during night-sleep. rRR and EEG mean frequency curves were smoothed using the moving average method over a five-point span.<sup>19</sup>

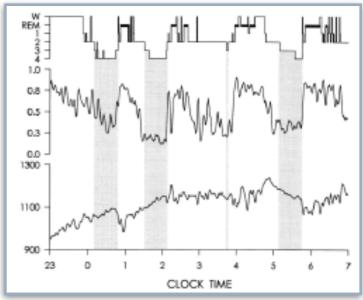


Fig. 3: Profiles of minute interbeat autocorrelation coefficient (rRR) and of RR interval together with sleep stage pattern in one subject. Slow wave sleep (stage 3 and 4) lies in shaded areas. rRR and RR curves were smoothed using the moving average method over a five-point span.<sup>20</sup>

## Sleep Monitoring with Vyvo Technology Wearables

As reviewed above, PPG is a convenient and effective method for monitoring and reporting sleep quality, but wrist PPG quality is far lower than finger PPG quality. Wearables from Vyvo Technology utilize the highest quality wrist PPG sensors and most powerful Analog Front End chips, paired with the most advanced Digital Signal Processing technologies. This enables the best possible wrist-based PPG. Also equipped with a motion sensor, Vyvo wearables employ actigraphy for improved, more accurate sleep monitoring.



Through PPG sensors and a proprietary back-end algorithm, wearables from Vyvo Technology also obtain and record accurate results of respiration rate, heart rate, heart rate variability (HRV), SpO2, etc., during sleep. With a built-in temperature sensor, the wearables record tiny changes of the user's body temperature during sleep. Users and medical professionals alike can review all data and results recorded during sleep for further analysis. Vyvo's Al summarizes all results captured by wearables, providing accurate sleep analysis results and professional insight. With Vyvo Technology, it's impressively easy for users to monitor and improve their sleep quality.

#### **Legal Disclaimer**

Unless otherwise specified, Vyvo Technology wearables and related services are not medical devices and are not intended to diagnose, treat, cure, or prevent any disease. With regard to accuracy, Vyvo Technology has developed products and services to track certain wellness information as accurately as reasonably possible. The accuracy of Vyvo Technology products and services is not intended to be equivalent to medical devices or scientific measurement devices.

Consult your doctor before use if you have any pre-existing conditions that might be affected by your use of any Vyvo Technology product or service.



#### **Useful Terms**

Actigraphy: The use of wrist-worn accelerometry devices that measure movement to estimate sleep.

**Electrocardiogram (ECG):** Used to measure and analyze electrical activity of the heart to detect abnormalities or heart arrhythmias.

**Heart Rate Variability (HRV):** Variation in the time interval between heartbeats, measured in milliseconds. High variability — for example a low heart rate upon waking and a higher rate during exercise — is considered a hallmark of good health.

**Photoplethysmography (PPG)**: An optical way to measure blood volume changes in a bed of tissue, such as a finger or earlobe. Obtained by illuminating the skin and measuring light absorption.

#### References

- (1) Wikipedia entry, "Sleep", https://en.wikipedia.org/wiki/Sleep. Accessed 11-22-21.
- (2) Ibid.
- (3) Peever J, Fuller PM. The Biology of REM Sleep. Curr Biol. 2017 Nov 20;27(22):R1237-R1248. doi: 10.1016/j.cub.2017.10.026. PMID: 29161567.
- (4) Rasch B, Born J. About sleep's role in memory. Physiol Rev. 2013 Apr;93(2):681-766. doi: 10.1152/physrev.00032.2012. PMID: 23589831; PMCID: PMC3768102.
- (5) Time.com, "Why Dreaming May Be Important for Your Health", <a href="https://time.com/4970767/rem-sleep-dreamshealth/">https://time.com/4970767/rem-sleep-dreamshealth/</a>. Accessed 9-03-2022.
- (6) Sterpenich V, Schmidt C, Albouy G, Matarazzo L, Vanhaudenhuyse A, Boveroux P, Degueldre C, Leclercq Y, Balteau E, Collette F, Luxen A, Phillips C, Maquet P. Memory reactivation during rapid eye movement sleep promotes its generalization and integration in cortical stores. Sleep. 2014 Jun 1;37(6):1061-75, 1075A-1075B. doi: 10.5665/sleep.3762. PMID: 24882901; PMCID: PMC4015380.
- (7) Siegel JM, Rogawski MA. A function for REM sleep: regulation of noradrenergic receptor sensitivity. Brain Res. 1988 Nov;472(3):213-33. doi: 10.1016/0165-0173(88)90007-0. PMID: 3066435; PMCID: PMC9050241.
- (8) Cai DJ, Mednick SA, Harrison EM, Kanady JC, Mednick SC. REM, not incubation, improves creativity by priming associative networks. Proc Natl Acad Sci U S A. 2009 Jun 23;106(25):10130-4. doi: 10.1073/pnas.0900271106. Epub 2009 Jun 8. PMID: 19506253; PMCID: PMC2700890.
- (9) Endo T, Roth C, Landolt HP, Werth E, Aeschbach D, Achermann P, Borbély AA (1998). "Selective REM sleep deprivation in humans: Effects on sleep and sleep EEG". The American Journal of Physiology. 274 (4 Pt 2): R1186–1194. doi:10.1152/ajpregu.1998.274.4.R1186. PMID 9575987
- (10) Sleep Foundation website, <a href="https://www.sleepfoundation.org/baby-sleep/baby-sleep-cycle">https://www.sleepfoundation.org/baby-sleep/baby-sleep-cycle</a> Accessed 09-02-2022.
- (11) Whitehurst LN, Cellini N, McDevitt EA, Duggan KA, Mednick SC. Autonomic activity during sleep predicts memory consolidation in humans. Proc Natl Acad Sci U S A. 2016 Jun 28;113(26):7272-7. doi: 10.1073/pnas.1518202113. Epub 2016 Jun 13. PMID: 27298366; PMCID: PMC4932927.
- (12) See, for example, Shigeta H, Shigeta M, Nakazawa A, Nakamura N, Yoshikawa T. Lifestyle, obesity, and insulin resistance. Diabetes Care. 2001 Mar;24(3):608. doi: 10.2337/diacare.24.3.608. PMID: 11289495.
- (13) Wikipedia entry, "Sleep Deprivation," https://en.wikipedia.org/wiki/Sleep\_deprivation. Accessed 11-24-21.
- (14) Domínguez F, Fuster V, Fernández-Alvira JM, Fernández-Friera L, López-Melgar B, Blanco-Rojo R, Fernández-Ortiz A, García-Pavía P, Sanz J, Mendiguren JM, Ibañez B, Bueno H, Lara-Pezzi E, Ordovás JM. Association of Sleep Duration and Quality With Subclinical Atherosclerosis. J Am Coll Cardiol. 2019 Jan 22;73(2):134-144. doi: 10.1016/j.jacc.2018.10.060. PMID: 30654884.

- (15) Senaratna CV, Perret JL, Lodge CJ, Lowe AJ, Campbell BE, Matheson MC, Hamilton GS, Dharmage 15 SC. Prevalence of obstructive sleep apnea in the general population: A systematic review. Sleep Med Rev. 2017 Aug;34:70-81. doi: 10.1016/j.smrv.2016.07.002. Epub 2016 Jul 18. PMID: 27568340.
- (16) Ma Y, Sun S, Zhang M, Guo D, Liu AR, Wei Y, Peng CK. Electrocardiogram-based sleep analysis for sleep apnea screening and diagnosis. Sleep Breath. 2020 Mar;24(1):231-240. doi: 10.1007/s11325-019-01874-8. Epub 2019 Jun 21. PMID: 31222591; PMCID: PMC6925360.
- (17) Kwon S, Kim H, Yeo WH. Recent advances in wearable sensors and portable electronics for sleep monitoring. *Iscience*. (2021) 24:102461. doi: 10.1016/j.isci.2021.102461
- (18) Otzenberger H, Simon C, Gronfier C, Brandenberger G. Temporal relationship between dynamic heart rate variability and electroencephalographic activity during sleep in man. Neurosci Lett. 1997 Jul 4;229(3):173-6. doi: 10.1016/s0304-3940(97)00448-5. PMID: 9237486.
- (19) Ibid.
- (20) bid.





# Monitoring with Vyvo Technology Wearables Devices

