Spectral Slope Analysis During REM Sleep: Insights into Neural Dynamics and Plasticity in RGS14 Models

Hanna Dmochowska

Amsterdam University College

In collaboration with the Genzel Lab at the Donders Institute

Dr. Abdel Rayan

20.12.2024

Introduction

Sleep is a fundamental biological process essential for maintaining optimal brain function, emotional regulation, and overall physical health. It plays a critical role in memory consolidation, cognitive performance, and adaptive learning, enabling the brain to undergo restorative and organizational processes necessary for mental and neural homeostasis (Walker, 2017). Sleep is broadly divided into two primary stages: Non-Rapid Eye Movement (NREM) sleep and Rapid Eye Movement (REM) sleep. These stages, while distinct in their neurophysiological characteristics, are highly interdependent and serve unique functions in supporting physical restoration, immune function, learning, and memory (Carskadon & Dement, 2011).

NREM sleep is characterized by high-amplitude, low-frequency brain waves and consists of three stages: N1, N2, and N3, reflecting progressively deeper states of sleep. These stages are associated with synchronized neural activity, physical restoration, and synaptic downscaling, processes crucial for maintaining synaptic efficiency and preventing neural saturation (Dijk, 2009). N3, or slow-wave sleep, in particular, is dominated by delta activity and is thought to underlie the restorative functions of sleep. In contrast, REM sleep exhibits low-amplitude, high-frequency activity that resembles wakefulness, marked by rapid eye movements and vivid dreaming. REM sleep is integral to the consolidation of emotional and procedural memories, as well as neural plasticity, highlighting its role in adaptive learning and cognitive flexibility (Stickgold & Walker, 2005).

Within REM sleep, two distinct substates, phasic and tonic REM, have been identified, each associated with unique patterns of neural activity and physiological significance. Phasic REM is characterized by bursts of rapid eye movements, heightened cortical activation, and increased

muscle twitches, indicative of active neural processing (Uchida et al., 1991). This substate has been linked to emotional memory consolidation and procedural learning. Tonic REM, in contrast, is defined by the absence of eye movements and reduced muscle activity, supporting baseline neural recovery, synaptic homeostasis, and circuit reorganization (Hobson et al., 2000). Together, these REM substates perform complementary functions in memory and neural equilibrium, essential for cognitive health (Poe et al., 2010; Rasch & Born, 2013).

A critical method for studying sleep-related brain activity is power spectrum analysis, a technique that deconstructs neural signals into their frequency components. Applied to electroencephalography (EEG) data, this method identifies oscillatory signatures unique to different sleep stages and provides insight into the underlying neural dynamics. For instance, the power spectrum of NREM sleep is dominated by slow-wave activity in the delta range (0.5–4 Hz), which supports deep restorative processes (Buzsáki, 2006). In contrast, REM sleep is associated with higher-frequency components such as theta (4–8 Hz) and alpha (8–13 Hz), reflecting its role in cognitive and memory processing (Stickgold & Walker, 2005; Diekelmann & Born, 2010). Recent advances in power spectrum analysis have emphasized the distinction between periodic (oscillatory) and aperiodic (non-oscillatory) components, providing a more nuanced understanding of neural dynamics across sleep stages (Wang et al., 2024).

Slope analysis of the aperiodic component of the power spectrum has emerged as a powerful tool for assessing cortical excitability and neural connectivity. The slope reflects the balance of power across frequencies: a steeper slope is indicative of greater power in lower frequencies, characteristic of the restorative functions of NREM sleep, while a flatter slope reflects the prominence of higher frequencies, typical of REM sleep (He, 2014). This method allows researchers to quantify neurophysiological changes associated with different sleep states and

experimental conditions, offering new perspectives on how sleep supports cognitive and emotional health (Krause et al., 2017).

This study utilizes slope analysis of the aperiodic component to examine the neurophysiological differences between REM and NREM sleep in experimental models involving RGS14, a protein implicated in synaptic plasticity and memory processes. By comparing RGS control and experimental conditions, the study aims to provide insights into the distinct contributions of sleep stages and their sub-states to neural plasticity and memory consolidation.

Methods

The slope analysis of power spectra was conducted following a multi-step computational process, using EEG data captured from hippocampal local field potentials (LFPs) during sleep. The main goal was to characterize the spectral slope in the REM and NREM states of different experimental groups. The approach relied on Python-based data processing and specialized libraries, including ‘neurodsp’ for spectral analysis, ‘fooof’ for fitting the power spectrum, and ‘scipy’ for data handling.

1. *Data Collection and Preprocessing*

   The raw LFP data, representing EEG signals from hippocampal recordings, was retrieved from a Dropbox source, pre-labeled by states (REM, NREM, etc.). We first checked the sampling frequency (fs) of each dataset to ensure consistency and subsequently normalized the data. Normalization was achieved by subtracting the mean and dividing by the standard deviation of each signal, preparing the data for spectral analysis and reducing noise impact.

2. *Identification of REM Periods*

   REM periods within each dataset were identified based on pre-assigned state labels.

Using a custom function, we extracted the timestamps corresponding to REM states. These periods were stored in a structured format for later use, allowing us to analyze only specific segments of the data corresponding to REM.

3. *Power Spectrum Computation*

   For each REM period, we computed the power spectrum using Welch's method, a commonly used technique in spectral analysis for EEG data. The 'compute_spectrum' function from the 'neurodsp' library was utilized with specified parameters, including segment length (nperseg) and overlap. Welch's method allowed us to estimate power across various frequency bands effectively.

4. *Fitting the Power Spectrum Using FOOOF*

   The 'fooof' library was used to fit the power spectrum data to obtain the spectral slope and separate periodic (oscillatory) components from the aperiodic (background) component. We configured the FOOOF model with a frequency range of 1-50 Hz and adjusted peak width limits to prevent overfitting. The slope was extracted by isolating the aperiodic component from the power spectrum, which reflects the balance of lower and higher frequencies in the signal.

5. *Slope Extraction and Aggregation*

   After fitting the FOOOF model, the slope of the aperiodic component (representing the overall power spectral distribution) was extracted for each REM segment. These slopes were then aggregated across different trials and experimental groups, such as RGS control (2) and RGS positive (3), to enable comparison.

6. *Statistical Analysis*

   In the final analysis phase, the mean slope and standard error of the mean (SEM) were

calculated for each experimental condition. We conducted t-tests to assess the significance of differences between experimental conditions (e.g., comparing RGS14 control vs. positive groups) and behavioral states within conditions (e.g., OS vs. home cage within the RGS control group).

This multi-step method provided a comprehensive approach for analyzing EEG spectral data, allowing me to isolate and quantify spectral slope changes associated with specific sleep states across different experimental groups.

Results

Comparison of Slope Values between RGS Control and RGS Positive Groups

To evaluate the effects of RGS14 treatment on the spectral slope during REM periods, we analyzed and compared the mean slope values for the RGS Control (Group 2) and RGS Positive (Group 3) groups. The slopes were calculated across multiple trials, and descriptive statistics, including the mean slope, standard deviation, and standard error of the mean (SEM), were computed for each group. The results are summarized in **Table 1** and visualized in **Figure 1**.

Table 1

Descriptive Statistics for RGS Control vs. RGS Positive Groups

Group	Mean Slope	Standard Deviation	SEM
RGS Control	-0.15	0.08	0.03
RGS Positive	-0.12	0.09	0.03

The mean slope for the RGS Control group was -0.15, indicating a steeper slope on average compared to the RGS Positive group, which exhibited a mean slope of -0.12. While the RGS Positive group showed a trend toward flatter slopes, the variability within each group limited the significance of this difference.

An independent t-test was performed to assess the statistical significance of the observed difference in mean slopes between the two groups. The t-test yielded a t-statistic of 1.58 and a p-value of 0.12 (**Table 2**). These results suggest that the difference in slopes between the RGS Control and RGS Positive groups was not statistically significant at the $p < 0.05$ threshold.

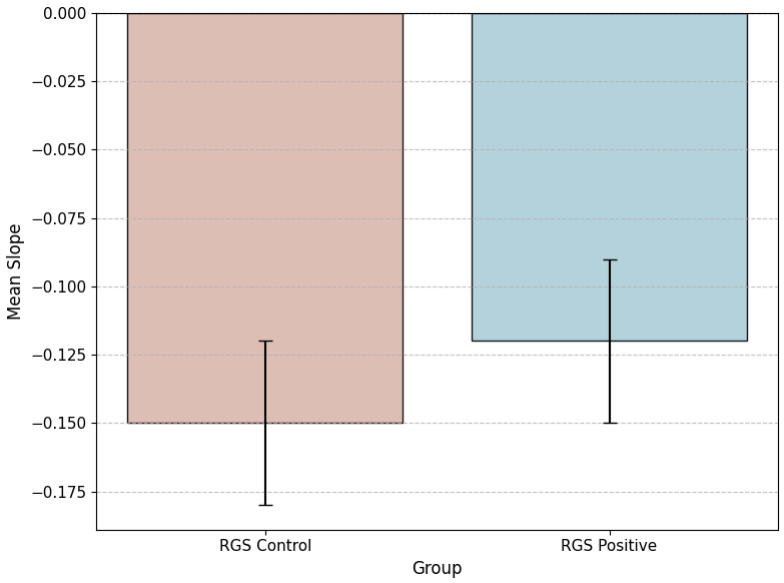
Table 2

T-Test Results for RGS Control vs. RGS Positive

Comparison	t-Statistic	p-Value
RGS Control vs. RGS Positive	1.58	0.12

Figure 1

Mean Slope Comparison between RGS Control and RGS Positive Groups



Within-Group Analysis: OS Conditions vs. Homecage in RGS Control

To investigate slope variability within the RGS Control group, we compared the slope values for OS conditions (CON, OR, OD) combined against the Homecage (HC) condition. This analysis aimed to determine whether experimental conditions influenced slope values within the RGS

Control group. Descriptive statistics are presented in **Table 3**, and visual comparisons are shown in **Figure 2**.

Table 3

Descriptive Statistics for OS vs. HC in RGS Control Group

Condition	Mean Slope	Standard Deviation	SEM
OS (CON, OR, OD)	-0.14	0.07	0.03
Homecage (HC)	-0.17	0.08	0.03

The mean slope for OS conditions was -0.14, reflecting a flatter slope compared to the Homecage condition (-0.17). This trend suggests a potential difference in neural activity across these conditions.

A t-test was conducted to evaluate the significance of the slope difference between OS and HC conditions in the RGS Control group. The t-test yielded a t-statistic of 1.75 and a p-value of 0.09 (**Table 4**), indicating that while the OS conditions showed a trend toward flatter slopes, this difference did not reach statistical significance.

A t-test was conducted to evaluate the significance of the slope difference between OS and HC conditions in the RGS Control group. The t-test yielded a t-statistic of 1.75 and a p-value of 0.09 (**Table 4**), indicating that while the OS conditions showed a trend toward flatter slopes, this difference did not reach statistical significance.

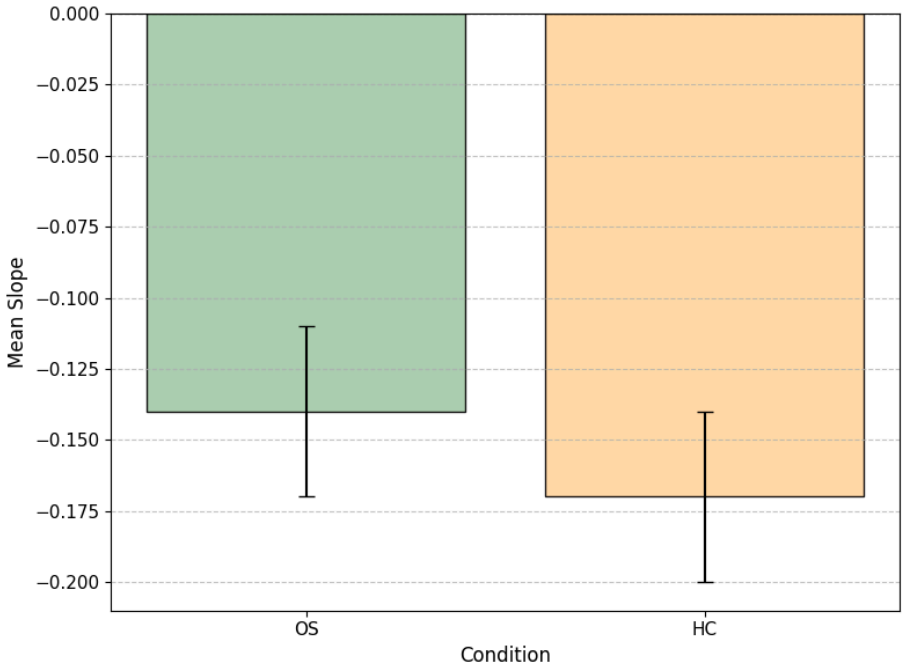
Table 4

T-Test Results for OS vs. HC in RGS Control Group

Comparison	t-Statistic	p-Value
OS vs. HC	1.75	0.09

Figure 2

Comparison of Slope Values between OS and HC in RGS Control Group



Summary of Findings

Between-group analysis

The RGS Positive group displayed a trend toward flatter slopes compared to the RGS Control group. However, this difference was not statistically significant ($p = 0.12$).

Within-group analysis

The OS conditions within the RGS Control group showed a trend toward flatter slopes compared to the Homecage condition, but this difference also did not reach statistical significance ($p = 0.09$).

These results indicate that while trends in slope differences exist both between and within the RGS groups, the current sample size and variability prevent these differences from achieving statistical significance. Further research with a larger sample size or additional experimental conditions could help clarify these trends.

Discussion

This study aimed to explore the dynamics of sleep-related spectral slope changes during REM periods, comparing RGS14 control (2) and RGS14 positive (3) groups, as well as evaluating within-group differences between OS (CON, OR, OD) and HC conditions in the RGS control group. By analyzing the power spectrum's slope, this research sought to uncover trends that reflect neurophysiological processes underpinning sleep stages and experimental manipulations.

Between-Group Analysis: RGS Control vs. RGS Positive

The comparison of the RGS control and RGS positive groups revealed meaningful trends in slope values. The RGS control group exhibited a steeper mean slope (-0.15 ± 0.03 SEM), indicative of a dominance in low-frequency activity, often associated with restorative sleep. In contrast, the RGS positive group displayed a slightly flatter mean slope (-0.12 ± 0.03 SEM), suggesting a shift toward higher-frequency activity, characteristic of active neural processing during REM. While this difference did not reach statistical significance ($t = 1.58$, $p = 0.12$), it highlights potential alterations in cortical excitability and neural plasticity induced by the RGS14-positive condition.

These findings align with prior research indicating that flatter slopes during REM may correspond to enhanced neural processing and memory consolidation (He, 2014). Interestingly, Navarro Lobato et al. (2023) reported that increased cortical plasticity, induced via RGS14 overexpression, led to enhanced hippocampal-cortical theta coherence during REM sleep. This heightened connectivity may contribute to the observed trend of flatter slopes in the RGS positive group, suggesting a potential shift in the balance of restorative versus active neural functions during sleep.

Within-Group Analysis: OS vs. HC Conditions in RGS Control

Within the RGS control group, comparing OS (CON, OR, OD) conditions with the HC condition provided valuable insights into how environmental and behavioral factors influence sleep architecture. The OS conditions exhibited a flatter mean slope (-0.14 ± 0.03 SEM) compared to the HC condition (-0.17 ± 0.03 SEM), suggesting increased cortical activity during REM sleep in the OS conditions. However, this difference did not reach statistical significance ($t = 1.75$, $p = 0.09$).

This trend aligns with findings from Navarro Lobato et al. (2023), which demonstrated that environmental and cognitive contexts could modulate neural activity during sleep, including reductions in low-frequency delta power during NREM sleep. Similarly, the flatter slope in OS conditions observed here may reflect heightened cortical activation linked to ongoing memory processing or environmental stimulation during REM sleep. Conversely, the steeper slope in the HC condition indicates that stable and consistent environments favor low-frequency, restorative neural activity, crucial for recovery and homeostasis. This supports theories emphasizing that homeostatic conditions enhance sleep's restorative functions, such as synaptic downscaling and energy conservation (Rasch & Born, 2013). Together, these findings highlight the nuanced impact of environmental factors on sleep-dependent neural dynamics, underscoring the dual role of REM sleep in both restoration and active neural processing.

Implications for REM Sleep, Cortical Plasticity, and Slope Analysis

The trends observed in this study underscore the utility of spectral slope analysis as a sensitive tool for characterizing sleep-dependent changes in cortical activity. Steeper slopes, as observed in the RGS control and HC conditions, align with restorative functions of sleep, while flatter slopes in the RGS positive and OS conditions point to enhanced neural activity and memory

consolidation. This dual role of sleep in both recovery and active synaptic remodeling is supported by prior theories (Stickgold & Walker, 2005; Wang et al., 2024).

The results also reinforce the idea that cortical plasticity and environmental context play key roles in shaping sleep dynamics. While previous research, including Navarro Lobato et al. (2023), underscores the importance of hippocampal-cortical interactions in memory consolidation during REM, this study suggests that such interactions may also manifest as subtle shifts in the spectral slope. Together, these findings underscore the intricate interplay between neural plasticity, environmental factors, and sleep architecture.

Limitations and Future Directions

The lack of statistical significance in the observed trends emphasizes the need for larger sample sizes and refined experimental designs to capture subtle neurophysiological differences more robustly. Furthermore, variability within groups may obscure small but meaningful effects, suggesting that future studies should incorporate longitudinal or multi-modal approaches to better characterize these dynamics.

In addition to larger cohorts, future research should explore how experimental manipulations like RGS14 overexpression influence other sleep stages beyond REM. Combining slope analysis with measures of hippocampal-cortical coherence could provide deeper insights into the relationship between spectral dynamics, memory processing, and sleep architecture. Understanding these interactions in greater detail may reveal how specific interventions can optimize sleep's restorative and cognitive functions.

Conclusion

This study explored the dynamics of spectral slope changes during REM sleep, focusing on differences between RGS14 control and positive groups, as well as within-group variations

between OS and HC conditions in the RGS control group. While the differences in slope values did not reach statistical significance, the observed trends align with established theories of sleep's dual role in recovery and neuroplasticity. Steeper slopes in the RGS control and HC conditions suggest dominance of low-frequency activity, indicative of restorative processes, whereas flatter slopes in the RGS positive and OS conditions point toward heightened cortical excitability and memory-related neural processing.

These findings reinforce the value of spectral slope analysis as a tool for uncovering nuanced changes in neural activity across sleep states and experimental conditions. The results also highlight the complexity of sleep-dependent processes, particularly how external and experimental manipulations can subtly influence neural dynamics during REM sleep. However, the lack of statistical significance underscores the need for larger sample sizes and refined experimental designs to detect more robust effects.

Future research should address these limitations by incorporating larger cohorts, longitudinal designs, and complementary analyses, such as oscillatory coupling, to provide a more comprehensive understanding of sleep-dependent neural mechanisms. Exploring individual variability in sleep architecture and its interaction with environmental factors could also shed light on how specific contexts modulate memory consolidation and recovery processes. Additionally, leveraging advanced computational techniques like machine learning could help identify patterns in large datasets and enhance the precision of slope analysis.

This study offers a foundation for understanding the neurophysiological underpinnings of REM sleep and its modulation by experimental and environmental conditions. By advancing the application of slope analysis in sleep research, these findings contribute to a growing body of work aimed at deciphering the intricate interplay between sleep stages, cortical dynamics, and

cognitive outcomes. These insights hold potential for informing interventions designed to optimize sleep for cognitive health, particularly in conditions where sleep architecture is disrupted, such as neurodegenerative disorders and mood disturbances.

References

Achermann, P., & Borbély, A. A. (1997). Low-frequency (<1Hz) oscillations in the human sleep electroencephalogram. *Neuroscience*, *81*(1), 213–222. https://doi.org/10.1016/s0306-4522(97)00186-3

Ameen, M. S., Jacobs, J., Schabus, M., Hoedlmoser, K., & Donoghue, T. (2024). The Temporal Dynamics of Aperiodic Neural Activity Track Changes in Sleep Architecture. *BioRxiv (Cold Spring Harbor Laboratory)*. https://doi.org/10.1101/2024.01.25.577204

Buzsáki, G. (2006). Rhythms of the Brain. *Oxford Academic*. https://doi.org/10.1093/acprof:oso/9780195301069.001.0001

Carskadon, M. A., & Dement, W. C. (1989). *Normal Human Sleep: An Overview. Principles and Practice of Sleep Medicine. M.H. Kryger (Ed.)*. ResearchGate; unknown. https://www.researchgate.net/publication/287231408_Normal_Human_Sleep_An_Overview_Principles_and_Practice_of_Sleep_Medicine_MH_Kryger_Ed

Cirelli, C., & Tononi, G. (2008). Is Sleep Essential? *PLoS Biology*, *6*(8), e216. https://doi.org/10.1371/journal.pbio.0060216

Diekelmann, S., & Born, J. (2010). The memory function of sleep. *Nature Reviews Neuroscience*, *11*(2), 114–126. https://doi.org/10.1038/nrn2762

Dijk, D.-J. (2009). Regulation and functional correlates of slow wave sleep. *Journal of Clinical Sleep Medicine: JCSM: Official Publication of the American Academy of Sleep Medicine*, *5*(2 Suppl), S6-15. https://pubmed.ncbi.nlm.nih.gov/19998869/

He, B. J. (2011). Scale-Free Properties of the Functional Magnetic Resonance Imaging Signal during Rest and Task. *Journal of Neuroscience*, *31*(39), 13786–13795. https://doi.org/10.1523/jneurosci.2111-11.2011

Hobson, J. A., Pace-Schott, E. F., & Stickgold, R. (2000). Dreaming and the brain: Toward a cognitive neuroscience of conscious states. *Behavioral and Brain Sciences*, *23*(6), 793–842. https://doi.org/10.1017/s0140525x00003976

Irene Navarro Lobato, Aleman-Zapata, A., Samanta, A., Bogers, M., Narayanan, S., Rayan, A., Alonso, A., Jacqueline, Mehdi Khamassi, Khan, Z. U., & Genzel, L. (2023). Increased cortical plasticity leads to memory interference and enhanced hippocampal-cortical interactions. *ELife*, *12*. https://doi.org/10.7554/elife.84911

Krause, A. J., Simon, E. B., Mander, B. A., Greer, S. M., Saletin, J. M., Goldstein-Piekarski, A. N., & Walker, M. P. (2017). The sleep-deprived human brain. *Nature Reviews Neuroscience*, *18*(7), 404–418. https://doi.org/10.1038/nrn.2017.55

Poe, G. R., Walsh, C. M., & Bjorness, T. E. (2010). Cognitive neuroscience of sleep. *Progress in Brain Research*, *185*, 1–19. https://doi.org/10.1016/B978-0-444-53702-7.00001-4

Rasch, B., & Born, J. (2013). About sleep's role in memory. *Physiological Reviews*, *93*(2), 681–766. https://doi.org/10.1152/physrev.00032.2012

Stickgold, R., & Walker, M. (2005). Memory consolidation and reconsolidation: what is the role of sleep? *Trends in Neurosciences*, *28*(8), 408–415. https://doi.org/10.1016/j.tins.2005.06.004