Changes over the night in REM-sleep microstructure. A hypothesis of similarity to changes in dream features reported in the literature

Umberto Barcaro, Massimo Magrini, and Paolo Paradisi

Institute for Information Science and Technologies, CNR, Pisa, Italy

Summary. The research aimed at a quantitative description of the changes in REM-sleep microstructure throughout the night. For this purpose, sleep recordings available on the public "PhysioNet" website were analyzed from a chronobiological perspective. This approach was suggested by the fact that two important properties of REM sleep determine its microstructure: the alternation between phasic and tonic microstates, and the presence of Slow Eye Movements in addition to Rapid Eye Movements. Although the examined recordings did not include data about dreams, a significant result of our analyses was the close similarity between the observed highly statistically significant changes in the microstructure and changes in basic dream features that are amply reported in the literature, including recall, word count, vividness and emotional content.

Keywords: Sleep Chronobiology, Dreaming Chronobiology, REM Sleep and Dreaming, REM-Sleep Microstructure, Dreaming and Eye Movements

1. Introduction

The research aimed to study the course of REM-sleep microstructure throughout the night, consisting in the alternation of sub-stages within the REM-sleep periods. In particular, we aimed to compare our results, only obtained by quantitative analyses of the EOG signals, with results, amply reported in the literature, about the chronobiology of basic dreaming features. We felt that this comparison could offer a contribution to the study of the complex relationship between dreaming and REM sleep.

Our approach was suggested by recent advancements in three research fields: the search for neural correlates of dreaming, the chronobiology of dreaming, and the inhomogeneity of REM sleep.

Regarding the neural correlates of dreaming, the analysis of polygraphic sleep recordings has allowed the observation of significant data (see Nielsen, 2000; Marzano et al., 2011; Chellappa et al., 2012; Nielsen et al., 2017; Siclari et al., 2017; Zhang & Wamsley, 2019; other references are found in a recent review by Scarpelli et al., 2021). Three alternative hypotheses can be distinguished (Scarpelli et al., 2015), based respectively on one dream generator for all sleep stages, on two distinct generators for NREM and REM sleep, or on the existence of covert REM sleep.

As to the chronobiology of dreaming, five different levels of oscillation have been observed (Nielsen, 2004): ultradian, circasemidian, circadian, circaseptan, and circatrigintan. In particular, as regards the changes throughout the night, an increase in the amount of dream recall and in the length of dream reports has been observed for the REM-sleep periods subsequent to the first, and similar changes have also been observed for other basic properties of the dreaming experience, including vividness and emotional content (this point is comprehensively highlighted in a review by Nielsen, 2010). In addition to perceptual and emotional features, also the structural properties of the dream experience change over the night (Cipolli et al., 2015). In the light of the continuity theory between dreaming and waking life (see, e.g., Hobson & Schredl, 2011) and in the light of the hypothesis of across-the-night changes in the features of this discontinuity (Schredl, 2003), marked differences have actually been found between early and late night (Malinowski & Horton, 2014). The chronobiological properties of dreaming are correlated with important issues, including metabolism (see Serin & Nilüfer, 2019), ageing (see Chellappa et al., 2009), personality factors (see Randler et al., 2017), and attention (see Valdez, 2019).

As to the inhomogeneity of REM-sleep, an important phenomenon is the alternation of "phasic" stages (characterized by the actual presence of Rapid Eye Movements) and "tonic" stages. (Of note, to avoid ambiguity due to the existence of REM-sleep sub-periods with no or poor REMs, in this paper the expression "REM sleep" will refer to the sleep stage and the term "REMs" will refer to rapid eye movements.) This alternation, which was observed more than fifty years ago (see Molinari & Foulkes, 1969), has subsequently been the subject of a vast amount of research. Among the most significant results are the following: the thalamocortical intrinsic loop active during REM sleep (Llinás & Paré, 1991) is specifically active during phasic stages (Wherle et al., 2007); thresholds for acoustic stimuli are lower during tonic stages (Ermis et al,. 2010); in patients affected by REM Sleep Behavior Disorder, phasic stages trigger a control mechanism for violent behavior (Frauscher et al., 2009); activity in the sensorimotor and heteromodal association

Corresponding address:
Umberto Barcaro, Istituto di Scienza e Tecnologie dell'Informazione, Consiglio Nazionale delle Ricerche, Pisa, Italy.
Email: umberto.barcaro@isti.cnr.it

Submitted for publication: December 2021
Accepted for publication: March 2023
DOI: 10.11588/ijodr.2023.1.84936

cortices alternate in multi-second periods during REM sleep (Chow et al., 2013). These and other data are amply discussed in a recent review (Simor et al., 2021).

A second form of inhomogeneity is seen in the occurrence of Slow Eye Movements (SEMs), whose frequency properties are similar to those that are typically present during sleep stage 1. The occurrence of SEMs in REM sleep, reported in Rechtschaffen & Kales' (1968) classic manual, has more recently been the object of specific studies (see Pizza et al., 2011; Danker-Hopfe et al., 2015). Thus, an analysis of the ElectroOculoGram (EOG) can allow a form of REM microstructure to be described, consisting in the alternation of four sub-stages, respectively characterized by poor presence of both REMs and SEMs, selective enhancement of SEMs, selective enhancement of REMs, and enhancement of both SEMs and REMs (Magrini et al., 2015).

We based our analyses on the criteria of easy repeatability and methodological simplicity. In fact, the results can be easily re-obtained because the EOG signals were downloaded from a useful database available from a public website (see the Methods Section), and the analysis procedures that we used have been published on the open portal of our Institute (website https://github.com/massimomagrini/rem_microstructure; Barcaro & Magrini, 2021). The applied method is conceptually and mathematically simple, being based on the calculation of two non-dimensional descriptors defined as the ratio of the quasi-instantaneous amplitude to the background amplitude of respectively the SEM and the REM components of the EOG signal. To assure the validity of the statistical analyses, we have taken care to apply exactly the same methodological criteria to all the subjects.

2. Methods

The analyses were carried out on polygraphic sleep recordings downloaded from the CAP sleep database (Terzano et al., 2001) of the PhysioNet website (Goldberger et al., 2000) (https://physionet.org/content/capslpdb/1.0.0/). These signals, although obtained for a specific purpose (the study of the Cyclic Alternating Pattern in NREM sleep), can also be useful for other kinds of sleep research. The recordings were obtained from 16 subjects (respectively indicated as n1, n2, …, and n16 on the website) with no neurological disorders and free of any drugs affecting the central nervous system. We did not analyze n12 and n16 because the data did not include EOG channels, nor n10 because the EOG signal presented some artifacts and the application of criteria for signal removal would have undermined the homogeneity of the analysis over the subjects. The labels of the EOG channels that we analyzed are: "ROC-LOC" (n1, n2, n3, n5, and n11), "EOG dx" (n4), "LOC-A1" (n6, n7, and n9), "EOG-R" (n8), "LOC" (n13, and n14), "EOG-L" (n15). The analysis procedures were written in the GNU-Octave language.

The considered REM-sleep periods were those indicated by the accurate sleep scoring reported on the website. We adopted the following preliminary criteria for all the analyses: 1) REM-sleep sub-epochs separated by short (4 min or less) intervals were assigned to the same REM period; 2) if short sub-epochs (4 min or less) were present in a REM-sleep period together with a much longer sub-epoch, the results obtained for the latter were assessed as valid for the whole REM-sleep period; otherwise, the results obtained for the sub-epochs were averaged. The number of REM-sleep

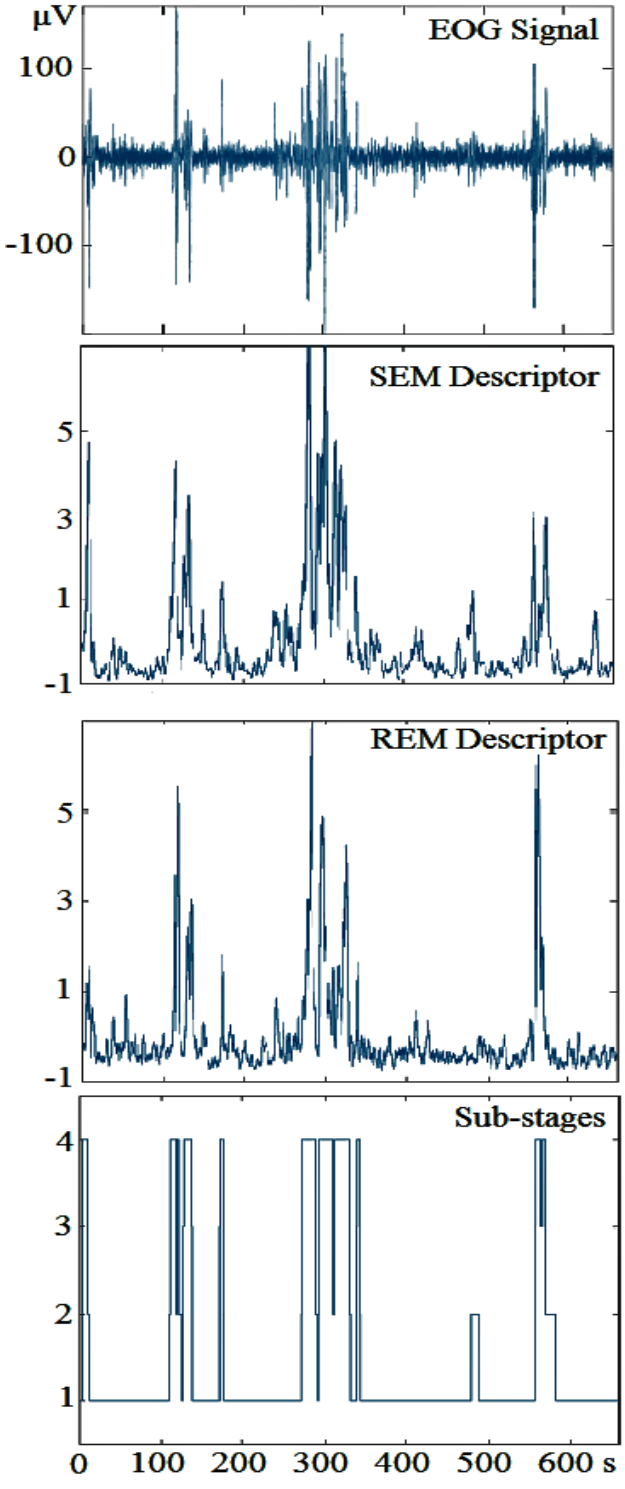

Figure 1. An example is given (subject n1, REM 1) of how the sub-stages were recognized. From top: the EOG signal, the correspondent non-dimensional SEM descriptor, the correspondent non-dimensional REM descriptor, and the resulting alternation of the sub-stages. In the descriptor graphs, the threshold value equal to 1 is particularly significant, because a necessary condition for a time interval being assessed as characterized by SEM / REM enhancement is the overcoming of this threshold at least once in the interval.

periods was either three (for n3), four (for n2, n4, n5, n8, n13, and n15), or five (for n1, n6, n7, n9, n11, and n14).

For each of the 13 subjects and each REM-sleep period (or sub-period considered), the properties of the microstructure were calculated in four steps:

1) Two band-pass filters (0.2-0.6 Hz, and 1-3 Hz) were applied to the EOG signal to obtain the SEM component and the REM component, respectively. These values of the cutoff frequencies were suggested by data in the literature (Smith et al.. 1971, Boukadoum & Ktonas, 1986, Magosso et al., 2007).
2) For each of the two components, the difference was calculated between the average amplitude over a moving window (ΔT = 2.5 s) and the average amplitude (AA) over the whole period (or sub-period) and then divided by AA. Thus, for each component, a non-dimensional descriptor was obtained.
3) An interval was recognized as characterized by SEM [or REM] enhancement if the following two conditions were met: for each instant of the interval, the SEM [or REM] descriptor was greater than low-threshold = 0; for at least one instant, the SEM [or REM] component was greater than high-threshold = 1. This method for the detection of enhancement intervals is similar to a method that has been applied for the recognition and quantitative description of the Cyclic Alternating Pattern (CAP) in NREM sleep (Navona et al., 2002). For the sake of simplicity, the values of ΔT, low-threshold, and high-threshold were the same as those applied to the analysis of the CAP.
4) Finally, the REM-sleep microstructure was described as the time alternation of four sub-stages, respectively characterized by: 1) no enhancement of either SEM or REM activity; 2) selective enhancement of SEM activity; 3) selective enhancement of REM activity; 4) enhancement of both REM and SEM activity. The percentage of time spent in each sub-stage was then calculated. By definition, this percentage was independent from the duration of the REM-sleep period (or sub-epoch).

3. Results

An example of the method applied for the quantitative description of the microstructure is given in Fig. 1. In addition to the EOG signal (subject n1, REM 1), the figure shows the correspondent SEM non-dimensional descriptor, the correspondent REM non-dimensional descriptor, and the time course of the instantaneous sub-stages.

For each of the four sub-stages, Fig. 2 shows the time course of the averaged percentages for the various REM-sleep periods (the average being calculated over the subjects). The trend is visually clear: the percentage for sub-stage 1 constantly decreases, while the percentages for sub-stages 3 and 4 (those characterized by REM enhancement) obviously tend to increase. As we will consider, this trend presents high statistical significance.

Table 1 reports the sum of the percentages of sub-stage 3 and sub-stage 4 for each REM-sleep period of the 13 subjects. For all the subjects (n = 13) except one (x = 1), an increase occurred from REM 1 to REM 2. If the binomial test is applied (n = 13, x = 1), the statistical significance is high (α = 0.0017). Interestingly, the decrease presented by the only exception (subject n1) was small and was followed by a remarkable increase in the subsequent REM-sleep period. Indeed, the increase from REM 1 to REM 3 (n = 13, x = 0) is even more significant (α = 0.0001). The increase from REM 2 to REM 3 is significant as well (n = 13, x = 2, α = 0.0112). The transition from REM 3 to REM 4 does not exhibit a significant trend, while the increase from REM 4 to REM 5 (n = 6, x = 0) is statistically significant (α = 0.0156).

4. Discussion

The quantitative analysis of REM-sleep microstructure highlighted a statistically significant trend that consisted in an increase, throughout the night, of the sub-stages characterized by enhancement of the rapid-eye-movement component of the EOG signal.

Table 1. For all the subjects and all the REM-sleep periods, the sum is reported of the time percentages of sub-stage 3 and sub-stage 4, i.e., the sub-stages that are characterized by enhancement of the rapid-eye-movement component of the EOG signal.

	REM 1	***REM 2***	***REM 3***	***REM 4***	***REM 5***
n1	15.48	15.31 (*)	22.13	22.26	23.66
n2	21.29	22.28	24.66	22.77 (*)	
n3	21.52	21.92	25.97		
n4	6.22	12.64	13.13	10.63 (*)	
n5	15.34	16.24	18.01	18.17	
n6	12.31	16.96	22.07	18.44 (*)	23.09
n7	12.61	18.32	20.95	18.23 (*)	23.5
n8	6.99	9.33	12.35	9.16 (*)	
n9	13.22	14.5	16.64	16.14 (*)	18.49
n11	13.9	16.07	17.31	20.39	22.91
n13	7.49	8.5	9.41	14.2	
n14	7.66	20.64	19.64 (*)	13.59 (*)	21.41
n15	9.51	24.3	15.45 (*)	21.13	

The asterisks indicate the decreases with respect to the immediately previous REM-sleep period.

The data that we analyzed included polygraphic signals and did not include mentation reports; however, the results indicate a close similarity between the chronobiological properties of REM-sleep microstructure and the chronobiological properties of basic dream features amply described in the literature. In fact, a chronobiological approach based on the features of REM-sleep microstructure may provide new insight into the complex relationship between dreaming and REM sleep.

The definition of microstructure is based on two important properties of REM-sleep: the alternation of tonic and basic phases, and the presence of SEMs in addition to REMs. We feel that the chronobiological properties of REM-sleep microstructure and their close relationship with dream properties can be a fruitful subject for further research, in particular in three directions: (a) a better understanding of the role of SEMs, (b) insight into other kinds of chronobiological factors, and (c) an analysis of the differences between individuals.

As to point (a), SEMs are importantly present in sleep stage N1, characterized by hypnagogic hallucinations: do SEMs play a somehow similar role in REM sleep? This question is connected to a more general question, which is still controversial, concerning a possible relationship between eye movements and the visual properties of dreaming (see Leclair-Visonneau et al., 2010).

As to point (b), while our study has focused on REM-sleep variations throughout the night, it would also be interesting to analyze the microstructural variations inside REM-sleep periods, and to see whether the transitions between different sub-stages are connected to the properties of dream recall in different instants of REM periods.

As to point (c), the sub-stage percentages, in spite of presenting chronobiological patterns common to the subjects, present variations in their range (for instance, the values reported in Table 1 for n4 and n8 are low). Do these differences depend on the subject or on the psychophysiological conditions of the subject in the recording night? Is the range of the respective percentages of the sub-stages connected to the features of the concomitant dreams?

References

Barcaro, U. & Magrini, M. (2021). A software Package for the Study of REM-Sleep Microstructure. Nota Tecnica, ISTI, CNR, Pisa. https://publications.cnr.it/doc/459327

Boukadoum, A.M., & Ktonas, P.Y. (1986). EOG Based Recording and Automatic Detection of Sleep Rapid Eye Movements: A Critical Review, and Some Recommendations". Psychophysiology, 23, 598-611.

Chellappa, S.L., Münch, M., Blatter, K., Knoblauch, V., & Cajochen, C. (2009). Does the Circadian Modulation of Dream Recall Modify with Age? Sleep, 32, 1201-1209. doi: 10.1093/sleep/32.9.1201

Chellappa, S. L., Munch, M., Knoblauch, V., & Cajochen, C. (2012). Age Effects on Spectral Electroencephalogram Activity Prior to Dream Recall. Journal of Sleep Research, 21, 247–256. doi: 10.1111/j.1365-2869.2011.00947.x

Chow, H.M., Horovitz, S.G., Carr, W.S., Picchioni, D., Coddington, N., Fukunaga, M., Xu, Y., Balkin. T.J., Duyn, J.H., & Braun, A.R. (2013) Rhythmic Alternating Patterns of Brain Activity Distinguish Rapid Eye Movement Sleep from Other States of Consciousness. PNAS 110:10305. doi: 10.1073/pnas.1313191

Cipolli, C., Guazzelli, M., Bellucci, C., Mazzetti, M., Palagini, L., Rosenlicht, N., & Feinberg. I. (2015). Time-of-Night Variations in the Story-Like Organization of Dream Experience Developed During Rapid Eye Movement Sleep. J Sleep Res, 24, 234-240. doi: 10.1111/jsr.12251

Danker-Hopfe, H., Gruber, G., Olbert, E., Dorffner, G., & Anderer, P. (2015). Variations in Microstructures of REM Sleep. Gender-Specific Differences and Age-Related Variation. Somnologie, 19, 12-21. doi:10.1007/s11818-015-0700-6

Ermis, U., Krakow, K., & Voss, U. (2010). Arousal Thresholds During Human Tonic and Phasic REM Sleep. Journal of Sleep Research, 19, 400-406. doi: 10.1111/j.1365-2869.2010.00831.x

Frauscher, B., Gschliesser, V., Brandauer, E., Ulmer, H., Poewe, W., & Högl, B. (2009).The Relation Between Abnormal Behaviors and REM Sleep Microstructure in Patients with REM Sleep Behavior Disorder. Sleep Medicine, 10, 174–181. doi: 10.1016/j.sleep.2008.01.003

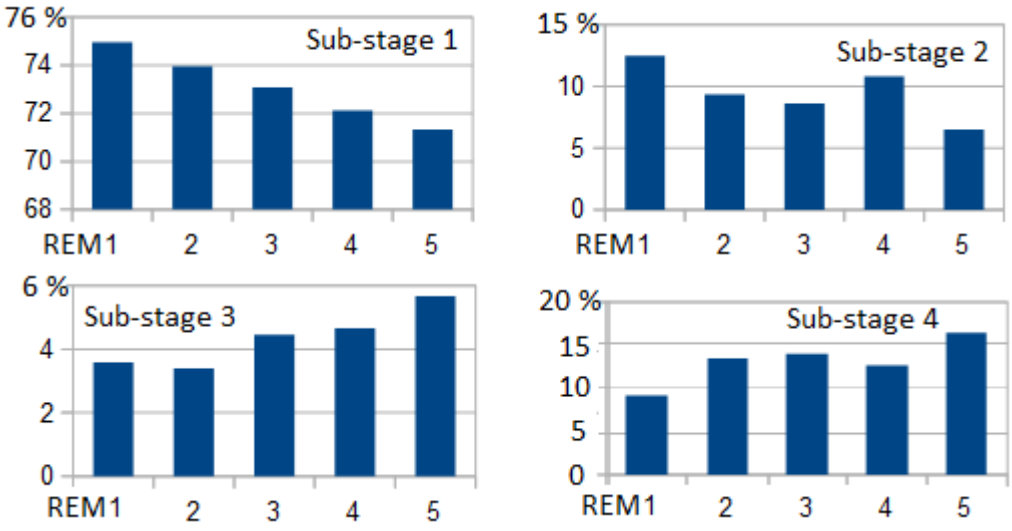

Figure 2. For the four sub-stages, the percentages, averaged over the subjects, are given for the successive REM-sleep periods

Goldberger. A.L., Amaral L.A., Glass, L., Hausdorff, J.M., Ivanov, P.C., Mark, R.G., Mietus, J.E., Moody, G.B., Peng, C.K., & Stanley, H.E. (2000). PhysioBank, PhysioToolkit, and PhysioNet: Components of a New Research Resource for Complex Physiologic Signals. Circulation, 10, e215-e220. doi: 10.1161/01.CIR.101.23.e215

Hobson, J.A., & Schredl, M. (2011). The Continuity and Discontinuity Between Waking and Dreaming: A Dialogue Between Michael Schredl and Allan Hobson Concerning the Adequacy and Completeness of these Notions. International Journal of Dream Research, 4, 3-7. doi: 10.11588/ijodr.2011.1.9087

Leclair-Visonneau, L., Oudiette, D., Gaymard B., Leu-Semenescu, S., & Arnulf. I. (2010). Do the Eyes Scan Dream Images During Rapid Eye Movement Sleep? Evidence from the Rapid Eye Movement Sleep Behaviour Disorder Model. Brain, 133, 1737-1746. doi: 10.1093/brain/awq110

Llinás, R.R., & Paré, D. (1991). Of Dreaming and Wakefulness. Neuroscience, 44, 521-553. doi:10.1016/0306-4522(91)90075-Y

Magosso, E., Ursino, M., Zaniboni, A., Provini, F,, & Montagna, P. (2007). Visual and Computer-Based Detection of Slow Eye Movements in Overnight and 24-h EOG Recording". Clinical Neurophysiology, 118, 1122-1133. doi:10.1016/j.clinph.2007.01.014

Magrini, M., Virgillito, A., Barcaro, U., Bonfiglio, L., Pieri, G., Salvetti, O., & Carboncini, M.C. (2015). An Automatic Method for the Study of REM Sleep Microstructure. IWCIM, 1-5. doi: 10.1109./IWCIM.2015.734706

Malinowski, J. E., & Horton, C. L. (2014). The Effect of Time of Night on Wake–Dream Continuity. Dreaming, 24, 253–269. doi: 10.1037/a0037817

Marzano, C., Ferrara, M., Mauro, F., Moroni, F., Gorgoni, M., Tempesta, D., Cipolli, C., & De Gennaro, L. (2011). Recalling and Forgetting Dreams: Theta and Alpha Oscillations During Sleep Predict Subsequent Dream Recall. Journal of Neuroscience, 31, 6674–6683. doi: 10.1523/JNEUROSCI.0412-11.2011

Molinari, S., & Foulkes, D. (1969). Tonic and Phasic Events During Sleep: Psychological Correlates and Implications. Perceptual and Motor Skills, 29, 343-368.

Navona, C., Barcaro, U., Bonanni, E., Di Martino, F., Maestri, M., & Murri, L. (2002). An Automatic Method for the Recognition and Classification of the A-Phases of the Cyclic Alternating Pattern". Clinical Neurophysiology, 113, 1826-1833. doi: 10.1016/S1388-2457(02)00284-5

Nielsen, T.A. (2000). A Review of Mentation in REM and NREM Sleep: "Covert" REM Sleep as a Possible Reconciliation of Two Opposing Models. Behav Brain Sci, 23, 851-866. doi: 10.1017/s0140525x0000399x

Nielsen, T.A. (2004). Chronobiological Features of Dream Production. Sleep Med. Rev., 8, 403–424. doi:10.1016/j.smrv.2004.06.005

Nielsen, T.A. (2010). Ultradian, Circadian, and Sleep-Dependent Features of Dreaming. In Kryger, M.H., Roth, T., & Dement, W.C. (Eds.) Principles and Practice of Sleep Medicine, Saint Louis, Elsevier – Saunders, 576-584.

Nielsen, T., Carr, M., Blanchette-Carriere, C., Marquis, L.-P., Dumel, G., Solomonova, E., Julien, S.-H., Picard-Deland, C., & Paquette, T. (2017). NREM Sleep Spindles are Associated with Dream Recall. Sleep Spindles & Cortical Up States, 1, 27–41. doi: 10.1556/2053.1.2016.003

Pizza, F., Fabbri, M., Magosso, E., Ursino, M., Provini, F., Ferri, R., & Montagna, P. (2011). Slow Eye Movements Distribution During Nocturnal Sleep. Clinical Neurophysiology, 122, 1556-1561. doi: 10.1016/j.clinph.2010.11.022

Randler, C., Schredl, M., & Göritz, A.S. (2017). Chronotype, Sleep Behavior, and the Big Five Personality Factors. SAGE Open, July-September 2017, 1–9. doi: 10.1177/2158244017728321

Rechtschaffen, A., & Kales, A. (1968). A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects. BI/BR, Los Angeles.

Scarpelli, S., D'Atri, A., Gorgoni, M., Ferrara, M. & De Gennaro, L. (2015). EEG Oscillations During Sleep and Dream Recall: State- or Trait-like Individual Differences? Front. Psychol. 6:605. doi: 10.3389/fpsyg.2015.00605

Scarpelli, S., Alfonsi, V., Gorgoni, M., Giannini, A.M., & De Gennaro, L. (2021). Investigation on Neurobiological Mechanisms of Dreaming in the New Decade. Brain Sci., 11, 220. doi: 10.3390/brainsci11020220

Schredl, M. (2003). Continuity Between Waking and Dreaming: A Proposal for a Mathematical Model. Sleep and Hypnosis, 5, 38–52.

Serin, Y., & Nilüfer, A.T. (2019). Effect of Circadian Rhythm on Metabolic Processes and the Regulation of Energy Balance. Annals of Nutrition and Metabolism, 74, 322-330. doi: 10.1159/000500071

Siclari, F., Baird, B., Perogamvros, L., Bernardi, G,, LaRocque, J,J,, Riedner, B., Boly, M., Postle, B.R., & Tononi, G. (2017) The Neural Correlates of Dreaming. Nature Neuroscience, 20, 872-878. doi: 10.1038/nn.4545

Simor, P., van der Wijk, G., Nobili, L., & Peigneux, P. (2020). The Microstructure of REM Sleep: Why Phasic and Tonic? Sleep Medicine Reviews, 52, 1-12. doi: 10.1016/j.smrv.2020.1013

Smith, J.R., Cronin, M., & Karacan, I. (1971). A Multichannel Hybrid System for Rapid Eye Movement Detection. Computers and Biomedical Research, 4, 275-290.

Terzano, M.G., Parrino, L., Sherieri, A., Chervin, R., Chokroverty, S., Guilleminault, C., Hirshkowitz, M., Mahowald, M., Moldofsky, H., Rosa, A., Thomas, R., & Walters, A. (2001). Atlas, Rules, and Recording Techniques for the Scoring of Cyclic Alternating Pattern (CAP) in Human Sleep. Sleep Med, 2, 537-553. doi: 10.1016/s1389-9457(01)00149-6

Valdez, P. (2019). Circadian Rhythms in Attention.Yale Journal of Biology and Medicine, 92, 81-92.

Wehrle, R., Kaufmann, C., Wetter, T.C., Holsboer, F., Auer, D.P., Pollmächer, T., & Czisch, M. (2007). Functional Microstates Within Human REM Sleep: First Evidence from fMRI of a Thalamocortical Network Specific for Phasic REM Periods. European Journal of Neuroscience, 25, 863-871. doi: 10.1111/j.1460-9568.2007.05314.x.

Zhang, J., & Wamsley, E.J. (2019). EEG Predictors of Dreaming Outside of REM Sleep. Psychophysiology, 2019;e13368. doi: 10.1111/psyp.13368