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Sleep-related hypermotor epilepsy and non-rapid eye movement parasomnias: Differences in the periodic and aperiodic component of the electroencephalographic power spectra

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Summary

Over the last two decades, our understanding of clinical and pathophysiological aspects of sleep-related epileptic and non-epileptic paroxysmal behaviours has improved considerably, although it is far from complete. Indeed, even if many core characteristics of sleep-related hypermotor epilepsy and non-rapid eye movement parasomnias have been clarified, some crucial points remain controversial, and the overlap of the behavioural patterns between these disorders represents a diagnostic challenge. In this work, we focused on segments of multichannel sleep electroencephalogram free from clinical episodes, from two groups of subjects affected by sleep-related hypermotor epilepsy ($N = 15$) and non-rapid eye movement parasomnias ($N = 16$), respectively. We examined sleep stages N2 and N3 of the first part of the night (cycles 1 and 2), and assessed the existence of differences in the periodic and aperiodic components of the electroencephalogram power spectra between the two groups, using the Fitting Oscillations & One Over f (FOOOF) toolbox. A significant difference in the gamma frequency band was found, with an increased relative power in sleep-related hypermotor epilepsy subjects, during both N2 ($p < .001$) and N3 ($p < .001$), and a significant higher slope of the aperiodic component in non-rapid eye movement parasomnias, compared with sleep-related hypermotor epilepsy, during N3 ($p = .012$). We suggest that the relative power of the gamma band and the slope extracted from the aperiodic component of the electroencephalogram signal may be helpful to characterize differences between subjects affected by non-rapid eye movement parasomnias and those affected by sleep-related hypermotor epilepsy.

KEYWORDS

aperiodic component, electroencephalography, non-rapid eye movement parasomnias, power spectrum, sleep-related hypermotor epilepsy, spectral slope

1 | INTRODUCTION

Common during both childhood and adulthood, non-rapid eye movement (NREM) parasomnias are sleep disorders defined as abnormal behaviours arising typically from sleep stage N3, and occasionally from N2 (American Academy of Sleep Medicine, 2014). They encompass: confusional arousals, sleepwalking and night terrors, also called "disorders of arousal", as well as lesser-known entities, such as sleep-related eating disorder, sexsomnia and sleep-related violence (American Academy of Sleep Medicine, 2014; Hrozanova et al., 2018). All types of NREM parasomnias share some basic features: (i) the episodes arise in the first part of the night or of the sleep period; (ii) the subject is unresponsive to the environment during the episodes; (iii) there is post-episodic amnesia for events (full or partial); (iv) electroencephalography (EEG) recordings show simultaneous sleep-like and wake-like features; (v) there are priming and precipitating factors. The dissociation between self-awareness and behaviour is a crucial feature of NREM parasomnias, and different studies have demonstrated a dissociation between wakefulness and sleep within different brain regions (Januszko et al., 2016; Sarasso et al., 2014; Terzaghi et al., 2009, 2012). This key point makes NREM parasomnias particularly fascinating disorders, and explains the possibly negative after-effects of the episodes, such as psychological distress, sleepiness, but especially the risk of self-injuries or harm for others, and their potential legal implications.

One of the most difficult challenges for sleep physicians and epileptologists is the differential diagnosis between NREM parasomnias and sleep-related hypermotor epilepsy (SHE). SHE seizures may arise in rather unconventional ways, as wandering, complex automatisms or vocalizations, often mistaken for parasomnias; likewise some NREM parasomnias may have particularly violent clinical features that can be mistaken for SHE seizures (Derry et al., 2006). Moreover, classical sleep parameters seem to be unchanged in subjects with both SHE and NREM parasomnias, in contrast with the presence of sleep instability, detectable by microstructure analysis, and arousal fluctuations (Zucconi & Ferini-Strambi, 2000). It is often impossible to find any evidence of ictal/interictal abnormalities during EEG investigations in SHE subjects (e.g. when seizures originate from the deep-seated cortex), and even detectable epileptic discharges are frequently masked by muscular artefacts (Provini et al., 1999; Tinuper & Bisulli, 2017; Tinuper et al., 2016). Several scalp sleep EEG studies, conducted in subjects with NREM parasomnias, highlighted increased sleep fragmentation and EEG slow-wave activity (SWA) abnormalities (Desjardins et al., 2017; Januszko et al., 2016). Castelnovo et al. (2016) demonstrated, with high-density EEG, the persistence of local sleep differences in SWA power during NREM and rapid eye movement (REM) sleep, and wakefulness, even during nights without clinical episodes, and they localized the local SWA decrease mainly to the cingulate and motor regions, supporting the theory that indicates the local arousals in these brain areas as the cause of NREM parasomnia motor behaviours (Terzaghi et al., 2012). These findings do not seem to make the process of diagnosis and differential diagnosis easier or quicker, and the gold-standard remains nocturnal video-polysomnography, an expensive, time-consuming and operator-dependent procedure, in which the video component is essential and, in association with the clinical features, allows to formulate the diagnosis by visual inspection.

While the oscillatory component has been investigated extensively, no attention was reserved to the changes of the aperiodic component of the power spectrum in subjects affected by SHE or NREM parasomnias. The aperiodic 1/f component of power spectra represents a significant fraction of the spontaneous electrical field potentials of the EEG recordings, and constitutes the arrhythmic and scale-free (no predominant temporal scale) brain activity (He et al., 2010). Although the aperiodic activity is the prevailing one when the oscillatory component is absent (Schaworonkow & Voytek, 2020), most of the studies are conducted on an ex ante basis, defining canonical frequency bands to investigate and ignore the arrhythmic "background" activity, thus failing to verify if the power changes detected are really driven by the oscillatory component, or are the result of the aperiodic signal, or a combination of the two (Haller et al., 2018). The aperiodic signal may correspond to both neural noise and physiologically relevant signals with a functional significance (Haller et al., 2018), and its dynamics manifest itself with changes dependent on task demands (He et al., 2010), cognitive states (Podvalny et al., 2015), aging (Voytek et al., 2015) and diseases (Peterson et al., 2017). The 1/f signal of the power spectrum may be characterized in terms of slope, namely the exponential decrease of power in a spectrogram as a function of frequency, and offset of the broadband power of the signal.

The aims of this study were: (i) to investigate the classical sleep EEG power spectral features; (ii) to extract the features of the aperiodic component (slope and offset); and (iii) to assess the presence of significant differences between the two groups of subjects, with NREM parasomnias or SHE. We also chose to focus on sleep stages N2 and N3 because of the well-known peculiar association of both disorders with slow-wave sleep, with events arising typically from sleep stage N3 and, occasionally, from N2 (American Academy of Sleep Medicine, 2014).

2 | MATERIALS AND METHODS

2.1 | Subjects

A total of 15 subjects with SHE (five males, mean age 32.8 ± 15.3 years) and 16 subjects with NREM parasomnia (eight males, mean age 29.5 ± 10.7 years) were enrolled at the Sleep Center and the Epilepsy Center of the University of Cagliari. The diagnosis was made according to the current diagnostic criteria, respectively, for SHE (Tinuper et al., 2016) and NREM parasomnias American Academy of Sleep Medicine, 2014). All subjects were aged ≥ 18 years. Exclusion criteria included the presence of other sleep disorders, neurological disease and psychiatric comorbidities, according to the DSM-V (American Psychiatric Association, 2013).

Demographic data, such as age, sex and current therapy, were evaluated by neurologists, experts in sleep medicine and epilepsy. All participants were drug-naïve for psychotropic medications (never

treated with any drug of the category). The study design was approved by the local ethics committee. The study was conducted according to the criteria set by the declaration of Helsinki, and each subject signed an informed consent before participating in the study.

2.2 | Polysomnographic analysis

All subjects underwent a full-night attended video-polysomnography (vPSG) recording at the sleep laboratory, according to the American Academy of Sleep Medicine (AASM) recommendations (Berry et al., 2017), using Morpheus MICROMED® recorder and SystemPlus Evolution for data acquisition.

The vPSG montage included EEG leads placed following the 10–20 international system (Fp2, F4, F8, C4, P4, T4, T6, O2, Fz, Cz, Pz, Fp1, F3, F7, C3, P3, T3, T5, O1, referred to A1 or A2), left and right electrooculography, electromyography of chin and lower limbs (tibialis anterior muscles), electrocardiography, nasal airflow, thoracic and abdominal respiratory effort, pulse-oximeter and microphone. The sampling rate was 256 Hz for all channels. All participants were asked to sleep uncovered, with allowance of a light sheet for comfort, in order to better observe any motor activity.

Polysomnographic recordings were scored according to the AASM criteria by neurologists, experts in sleep medicine (MF, MP, LT). The following sleep architecture data were collected: total bedtime (TBT), total sleep time (TST), sleep efficiency (SE), wakefulness after sleep onset (WASO), percentage of time in each sleep stage (N1, N2, N3, R), number of REM sleep episodes, arousal index (AI), periodic leg movements during sleep index (PLMSI), apnea–hypopnea index (AHI).

All video recordings were carefully analysed by experts in epilepsy and sleep medicine in order to detect minor and major events. In SHE subjects, minor events were defined as nose scratching, dystonic posture of feet or hands, hyperextension of limbs, rigid posture of upper or lower limbs, myoclonus, trunk flexion/extension, paroxysmal arousal, nocturnal wanderings and automatisms according to the current diagnostic criteria (Tinuper et al., 2016); while in subjects with NREM parasomnias, simple arousal movements and rising arousal movements were identified as minor events, according to the latest classification (Loddo et al., 2018). Major events were defined as complex hypermotor seizures in the SHE group (Tinuper et al., 2016), and as complex arousals with motor behaviours and walking movements in the NREM parasomnia group (Loddo et al., 2018).

2.3 | Preprocessing

Original raw data underwent multiple rounds of visual inspections by two of the authors (S.P., L.T.), and 25 epochs lasting 10 s each, for each sleep stage considered (N2 and N3), were retained through a process of visual exclusion of artefacts and generic discontinuities, using the freely available toolbox EEGLAB (Delorme & Makeig, 2004). All epochs were derived from the second sleep cycle, and were preceded by at least 120 s of artefact/minor event-free EEG activity. In the case of occurrence of major motor events, we secured to extract only epochs that were at least 1 hr apart from a preceding event, and 15 min apart from a following one. Our analysis included, therefore, 4 min and 10 s of EEG signal for each subject and for each of the two sleep stages, N2 and N3. The band-pass filtering procedure was performed using the "eegfilt" function provided by the EEGLAB toolbox (version 2020_0). The filtering procedure did not include the use of high-pass filter to remove drifts as it has been shown that minor but deleterious effects may be introduced (van Driel et al., 2021).

2.4 | Feature extraction

We extracted from the signal epochs the features characterizing: (i) the periodic component, namely the relative power of the delta (0.5–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), sigma (12–16 Hz), beta (16–32 Hz) and gamma (32–45 Hz) frequency bands (Hogan et al., 2020); and (ii) the parameters of the aperiodic component, namely the slope and the offset. The relative power for each of the six frequency bands was computed within MATLAB (The MathWorks, Natick, Massachusetts, USA, version R2020) as the ratio between the absolute band-specific power and absolute total power (between 1 and 45 Hz) using the power spectral density estimated using Welch's method, using Hamming windowing, set to obtain a 50% overlap, and with a number of FFT set to the next power of two greater than the length of each section.

We obtained, for each subject and epoch, a features vector of 19 entries, each of them representing the corresponding relative power, slope or offset of a single EEG channel. Starting from the matrix with the dimension equal to (number of subjects) × (number of epochs) × (number of channels) and averaging first across all channels and then across all 25 epochs, we obtained one value for each subject, which was used to compute medians, interquartile range (IQR) and the Mann–Whitney *U*-test.

The Fitting Oscillations & One Over f (FOOOF) toolbox (Haller et al., 2018) was used to compute the slope and the offset of power spectra (https://fooof-tools.github.io/fooof/index.html).

2.5 | Statistical analysis

Based on the characteristics of our data, namely two groups of subjects that can be considered as two independent samples and the continuous nature of the variables examined, we chose to use the Mann–Whitney *U*-test, often considered the non-parametric analogous of the *t*-test, in order to estimate whether the two populations of subjects differ, and the actual divergence of their medians. In consideration of the small sample size of the groups of subjects, we also calculated the effect sizes by means of the biserial rank correlation. With this approach, an absolute *r*-value = .10 is considered to represent a small effect, $r = .30$ represents a medium effect, and $r = .50$ represents a large effect (Conroy, 2012). The Mann–Whitney *U*-test was computed for each frequency band using Jamovi (version 1.1.9.0) available from https://www.jamovi.org, after performing an average across all channels and epochs.

We approached the multiple comparison problem lowering the critical value of p for significance with the Bonferroni correction. For the comparison of the periodic component, the critical value for an individual test was found dividing the familywise error rate (0.05) by the number of bands (six), the results were thus declared significant if they survived Bonferroni correction over the six bands ($p = .0083$). For the comparison of the aperiodic component, a critical p-value of .025 was used, because we made only two comparisons (offset and slope), for each sleep stage.

3 | RESULTS

3.1 | vPSG features

The SHE subjects showed significantly lower TST, higher amount of stages W and N1, and longer REM sleep latency ($p = .01$) compared with subjects with NREM parasomnia. The video analysis did not show significant differences between the two groups in the number of both minor and major motor events, specifically a small number of major motor events were detected in three SHE and two NREM parasomnia patients, respectively. Table 1 summarizes the vPSG parameters and results of video analysis in subjects with NREM parasomnia and in subjects with SHE.

3.2 | Periodic component

A significant difference between the groups was found for the gamma band relative power during N2, as well as during N3 (Table 2). No other difference survived Bonferroni correction. The relative power analysis of the gamma frequency band, respectively, during N2 and N3 sleep stages, is graphically shown also in Figure 1.

3.3 | Aperiodic component

No significant differences between NREM parasomnias and SHE subjects were found in offset of the power spectrum, both during N2 and N3 stages, while a significant higher slope was found for the NREM parasomnias group in sleep stage N3 only; see Figure 2 for a graphical representation of these results, and Table 3 for the corresponding statistics.

4 | DISCUSSION

4.1 | Periodic and aperiodic components of the EEG power spectra

Nocturnal vPSG is indispensable for making a precise diagnosis in subjects affected either by SHE or NREM parasomnias. While EEG is in general a tool with optimal accessibility and cost-effectiveness, a full-night attended vPSG, with its scoring process conducted by sleep medicine experts, is a more expensive and time-consuming procedure. Part of the research on SHE and NREM parasomnias focuses on a potential solution of the problem represented by the differential diagnosis, with the goal to identify electrophysiological biomarkers specific for each disease, besides existing questionnaires (Nobili et al., 2020). Similarly to most clinical and cognitive neuroscience studies, sleep studies focus on the so-called periodic activity, namely the rhythmic or oscillatory activity, organized in distinct frequency bands.

With a classical approach assessing changes in the different sleep EEG bands, we have detected a significant difference between SHE and NREM parasomnia regarding the relative power of the gamma band during sleep stages N2 and N3, higher in subjects with SHE. This finding should be interpreted in the light of the role of this band in the neurophysiological mechanisms of sleep. First of all, it should be mentioned that recent evidence supports that, even if probably generated by small neuronal groups, these fast rhythms can be detected in the scalp EEG, especially in subjects with different forms of epilepsy (Kobayashi et al., 2015; Zelmann et al., 2014). The gamma band does not seem to have been investigated earlier in the scalp EEG obtained from subjects with SHE. Our findings seem to indicate that, similarly to other forms of epilepsies (van Klink et al., 2016; Ohuchi et al., 2019), also in SHE the scalp EEG gamma band might be connected with the activities recorded intracerebrally in other conditions characterized by the onset of seizures at night (Grenier et al., 2003), and more research is needed in this direction.

It is important to emphasize that intracranially recorded gamma oscillations have been shown to be modulated by slow waves during slow-wave sleep, being enhanced during the surface-positive portion of the slow oscillations, and gamma activity seems to be strongly correlated with delta waves rather than with the epileptic activity (Valderrama et al., 2012). The association between the gamma band and SWA in the sleep EEG also allows to speculate about a possible role of the interaction between these two activities in the determinism of the frequent neurocognitive impairment found in subjects with SHE (Licchetta et al., 2018), in consideration of the importance of SWA within the framework of the so-called synaptic homeostasis hypothesis by Tononi and Cirelli (2003, 2006, 2012).

However, we also found a significant difference between SHE and NREM parasomnia for the aperiodic component during sleep stage N3. In contrast with the traditional view, the 1/f component of neural power spectra seems to represent both background noise and physiologically relevant signals and, considering that it incorporates the oscillatory component, it is important to take it into account in order to avoid misinterpretation of band-limited power differences (Haller et al., 2018). Recent experimental findings confirm the dynamism of the aperiodic component, showing how its parameters change depending on age (Schaworonkow & Voytek, 2020; Tran et al., 2020; Voytek et al., 2015), cognitive state (Podvalny et al., 2015) and disease (Peterson et al., 2017; Robertson et al., 2019). Furthermore, it was very recently demonstrated that the aperiodic component is characterized by strong

TABLE 1 vPSG features of NREM parasomnia subjects and SHE subjects

	NREM parasomnia ($n = 16$)		SHE ($n = 15$)		Mann–Whitney	
	Median	IQR	Median	IQR	*U*	*p*
Age, years	30.6	22.9–37.7	25.9	21.7–52.1	111.0	.741
TST, min	465.5	423.5–503.0	409.0	373–448	66.5	**.034**
SE, %	89.7	81.1–95.7	80.0	70–85.9	74.0	.070
Sleep latency, min	13.5	6.3–24–3	22.5	7.0–45	93.0	.295
AI	10.6	7.3–14.1	9.6	7.7–12.7	96.5	.363
WASO	30.0	12.1–64.3	73.5	38–126.5	63.5	**.025**
Stage N1, %	7.1	4.1–8.9	8.9	6.9–14.3	70.0	**.048**
Stage N2, %	42.3	33.2–45.6	37.8	26.7–48.8	110.5	.719
Stage N3, %	31.4	27.8–39.3	2.1	23.6–42.8	103.5	.526
Stage R, %	18.6	16.5–21.9	14.9	6.8–22.5	79.0	.108
REM sleep latency, min	87.8	71.1–124.4	184.5	92–264.5	48.0	**.004**
REM sleep episodes, number	4.0	3.0–4.8	4.0	3.0–4.0	91.0	.227
AHI	0.0	0.0	0.0	0.0	114.0	> .999
PLMSI	5.1	1.4–10.0	0.0	0.0	84.5	.153
Minor motor episodes, number	48.5	34.5–57.8	40.0	29.0–64.0	103.5	.526
Nose scratching	13	6.0–16.3	10	3.0–13.5	96.0	.352
Dystonic posture of feet or hands	3.0	0.75–5.25	2.0	1.0–9.0	115.0	.842
Hyperextension of limbs	3.5	1.75–5.25	4.0	1.50–5.50	110.0	.691
Rigid posture of upper/lower limbs	4.0	2.0–9.0	2.0	0.5–4.0	78.0	.097
Arching of the back	4.0	1.50–5.0	1.0	1.0–4.0	95.0	.326
Hips movements	15.5	2.0–26.3	13	9.0–20.0	119.0	.969
Myoclonus	0.0	0.0	0.0	0.0	113.0	.590
Paroxysmal arousal	0.0	0.0–1.25	0.0	0.0–1.5	120.0	1.0
Nocturnal wanderings	0.0	0.0–1.0	0.0	0.0–1.0	119.0	.963
Automatisms	2.0	0–6.25	1.0	0.0–4.0	101.0	.443
Major motor episodes, number	0.0	0.0	0.0	0.0	112.0	.643

AHI, apnea–hypopnea index; AI, arousal index; IQR, interquartile range; NREM, non-rapid eye movement; PLMSI, periodic leg movements during sleep index; REM, rapid eye movement; SE, sleep efficiency; SHE, sleep-related hypermotor epilepsy; TST, total sleep time; WASO, wakefulness after sleep onset.

Significant *p*-values (without Bonferroni correction) are marked in bold.

subject-specific properties, and its features may help to characterize and make inferences at the single subject level, with a better performance than that of the classical frequency bands (Demuru & Fraschini, 2020).

Taken together, these findings indicate the importance to consider the aperiodic component of the EEG power spectra as partly independent from oscillations, with its own physiological significance and dynamics. The possible use of its features for both diagnostic purposes (biomarkers) and bio-engineering clinical applications of brain fingerprint is also interesting. Robertson et al. (2019) identified for the first time differences in the aperiodic components of the EEG power spectrum in children with

TABLE 2 Results of the comparison of the relative power of the different EEG bands found in NREM Parasomnia and SHE, during sleep stages N2 and N3.

	NREM parasomnia ($n = 16$)		SHE ($n = 15$)		Mann–Whitney	Effect size
	Median	IQR	Median	IQR	*P*	Biserial rank correlation
N2 sleep stage						
Delta	0.654	0.576–0.676	0.616	0.518–0.681	.379	0.192
Theta	0.178	0.165–0.208	0.209	0.162–0.254	.520	0.142
Alpha	0.089	0.074–0.109	0.088	0.071–0.123	.800	0.058
Sigma	0.054	0.041–0.084	0.050	0.045–0.076	.984	0.008
Beta	0.033	0.021–0.050	0.040	0.028–0.060	.379	0.192
Gamma	0.005	0.003–0.007	0.011	0.008–0.014	**< .001**	**0.717**
N3 sleep stage						
Delta	0.860	0.762–0.900	0.792	0.749–0.854	.105	0.308
Theta	0.087	0.080–0.116	0.117	0.099–0.158	.093	0.358
Alpha	0.046	0.026–0.070	0.048	0.030–0.075	.401	0.183
Sigma	0.018	0.011–0.026	0.020	0.015–0.034	.281	0.233
Beta	0.005	0.004–0.009	0.009	0.007–0.013	.024	0.475
Gamma	0.001	0.0006–0.002	0.003	0.002–0.005	**< .001**	**0.800**

IQR, interquartile range; NREM, non-rapid eye movement; SHE, sleep-related hypermotor epilepsy.
Significant *p*-values (after Bonferroni correction) and "large" effect sizes (≥ 0.5) are marked in bold.

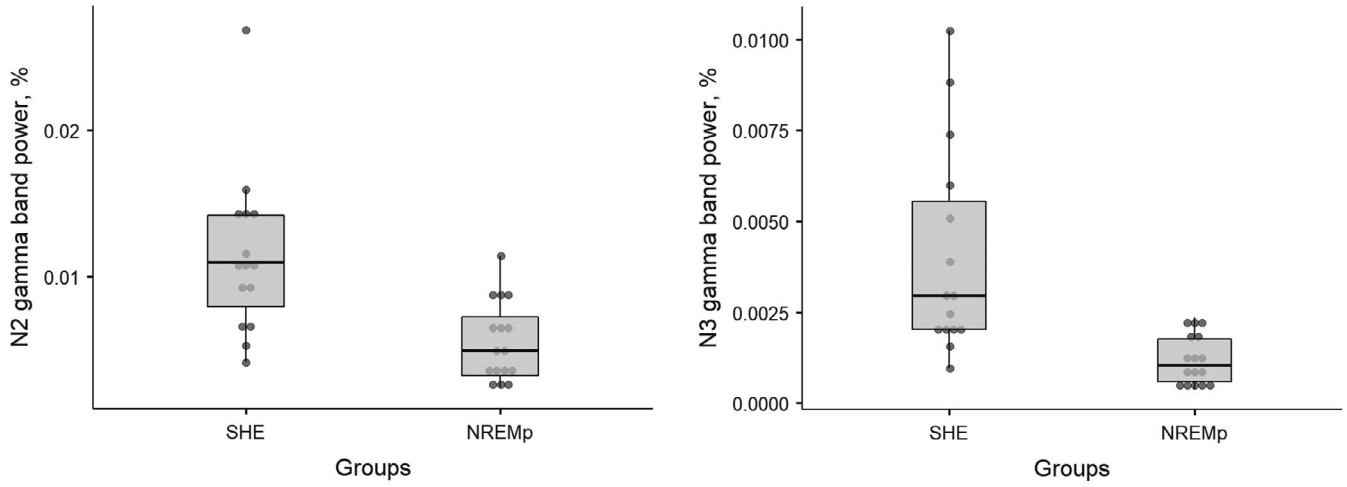

FIGURE 1 Scatterplot of the results for the gamma relative power during sleep stages N2 and N3. NREMp, NREM parasomnias; SHE, sleep-related hypermotor epilepsy

attention-deficit/hyperactivity disorder, proving that the slope is a reliable index of an increase of the low-frequency power, relative to the high-frequency power. Thus, this approach has potential clinical utility because it quantifies in a more comprehensive way the features of the EEG power spectrum and, for this reason, we decided to assess the spectral slope and offset in subjects affected by SHE and NREM parasomnias, with the aim to study the aperiodic features, looking for possible biomarkers. Indeed, we found a less steep slope of the EEG power spectrum in SHE than in NREM parasomnia, during sleep stage N3, pointing at a relative decrease in low-frequency activities and/or increase in high-frequency activities. It is premature to indicate the significantly lower slope in subjects affected by SHE, compared with subjects affected by NREM parasomnias, as a biomarker, but our findings seem to suggest that this can be a new approach for further research.

4.2 | Limitations and future steps

The major limitation of this preliminary/exploratory study is represented by the low number of subjects enrolled, due to the prevalence of SHE in the general population (SHE is a rare condition with

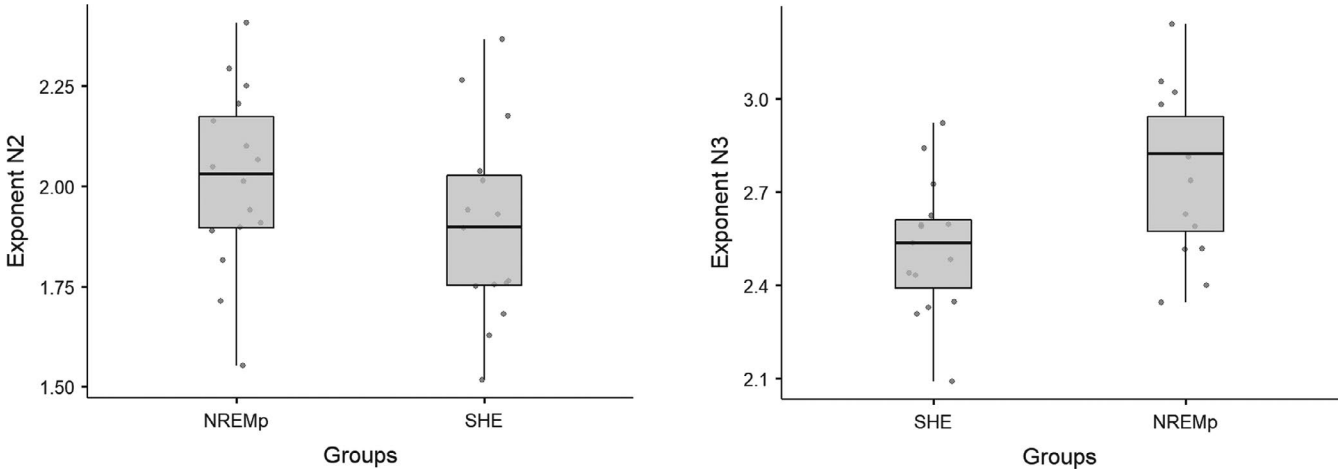

FIGURE 2 Scatterplot of the results for the slope (exponent) of the aperiodic component during sleep stages N2 and N3. NREMp, NREM parasomnias; SHE, sleep-related hypermotor epilepsy

TABLE 3 Results of the comparison of the offset and slope (exponent) of the EEG power spectrum in NREM parasomnia and SHE, during sleep stages N2 and N3

	NREM parasomnia ($n = 16$)		SHE ($n = 15$)		Mann–Whitney	Effect size
	Median	IQR	Median	IQR	*P*	Biserial rank correlation
N2 sleep stage						
Offset	1.91	1.82–2.07	1.89	1.57–2.07	.495	0.150
Slope	2.03	1.90–2.17	1.90	1.75–2.03	.163	0.300
N3 sleep stage						
Offset	2.74	2.55–2.86	2.56	2.38–2.72	.101	0.350
Slope	2.82	2.57–2.94	2.54	2.39–2.61	**.012**	**0.525**

IQR, interquartile range; NREM, non-rapid eye movement; SHE, sleep-related hypermotor epilepsy.
Significant *p*-values (after Bonferroni correction) and "large" effect sizes (≥ 0.5) are marked in bold.

an estimated prevalence of approximately 1.8/100,000; Menghi et al., 2018), and the need of strict inclusion/exclusion criteria (including comorbidities and treatments). The relatively small number of patients greatly limits the evaluation of the relationship between the periodic and aperiodic features derived from our analysis and disease severity markers.

It should also be mentioned the lack of a control group which, however, would have not been crucial for the direct comparison between the two clinical groups of subjects; however, it would have reinforced the considerations about the eventual possibility to use the parameters considered, the aperiodic component in particular, as biomarkers for the differential diagnosis between the two pathologies. Next steps include, therefore, the recruitment of a larger number of subjects and to extend the study to healthy controls, for a more detailed analysis of the parameters of interest, and the study of the possible correlation between periodic and aperiodic features and disease severity markers.

We should also consider that the eventual presence of night-to-night variability cannot be assessed with our single-session approach. Indeed, the rigorous selection of the epochs, as described in Materials and Methods, allows to believe that night-to-night variability might have a negligible impact on our findings; only a multi-session approach might address this point.

The averaging across all channels and epochs could be seen as a limitation because of the possible masking of significant results on single channels; however, the poor spatial resolution of 19-channel EEG recorded here would have represented a limitation too. On the contrary, we consider a strength the survival of significant differences in our results after averaging across all channels and epochs, as confirmation of the existence of an underlying significant global phenomenon. However, considering the value and the complexity of the single-channel approach, future steps might include a focused analysis on this aspect to complement the results obtained by averaging across all channels and epochs.

4.3 | Conclusions

The preliminary findings reported in this paper suggest that the gamma band of the scalp-recorded sleep EEG during NREM sleep

and a feature extracted from the aperiodic component, namely the slope, seem to convey physiological information that might help distinguishing SHE from NREM parasomnias; these features should be further investigated for their potential role as possible electrophysiological biomarkers (alone or in combination) to support the differential diagnosis in subjects with uncertain clinical features.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Author contributions

Sara M. Pani: study design, manuscript drafting, EEG power spectra analysis. Michela Figorilli: patient recruiting, sleep scoring and database collection. Ludovica Tamburrino: sleep scoring and database collection. Matteo Fraschini: EEG power spectra analysis, statistical assessment, manuscript revision. Raffaele Ferri: statistical assessment, manuscript revision, English editing. Monica Puligheddu: study design, manuscript revision, selection of subjects and clinical assessment.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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