SLEEP, 2025, 48, 1–11
https://doi.org/10.1093/sleep/zsae252
Advance access publication 25 October 2024
Original Article

Original Article

Spectral dynamics prior to motor events differ between NREM sleep parasomnias and healthy sleepers

Anna Castelnovo[1,2,3,*,†], Greta Mainieri[4,5,†], Giuseppe Loddo[6], Spyros Balafas[7,8], Chiara Brombin[7], Giulia Balella[4], Angelica Montini[4], Clelia Di Serio[2,7,9], Mauro Manconi[1,2,10] and Federica Provini[4,5,*]

[1]Sleep Medicine Unit, Neurocenter of Italian Switzerland, Ospedale Civico, Lugano, Ente Ospedaliero Cantonale (EOC), Switzerland,
[2]Faculty of Biomedical Sciences, University of Italian Switzerland, Lugano, Switzerland,
[3]Department of Psychiatric Neurophysiology, University Hospital of Psychiatry, University of Bern, Bern, Switzerland,
[4]Department of Biomedical and NeuroMotor Sciences, University of Bologna, Bologna, Italy,
[5]IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy,
[6]Department of Primary Care, Azienda AUSL di Bologna, Bologna, Italy,
[7]University Center for Statistics in the Biomedical Sciences, Faculty of Psychology, Vita-Salute San Raffaele University, Milan, Italy,
[8]Unit of PharmacoTherapy, Epidemiology and Economics, Groningen Research Institute of Pharmacy, University of Groningen, Groningen, The Netherlands,
[9]Clinical Trial Unit (CTU), Ente Ospedaliero Cantonale (EOC), Bellinzona, Switzerland and
[10]Department of Neurology, University Hospital, Inselspital, Bern, Switzerland

*Corresponding author. Federica Provini, IRCCS Institute of Neurological Sciences of Bologna, Bellaria Hospital, Via Altura 3, 40139 Bologna, Italy. Email: federica.provini@unibo.it; Anna Castelnovo, Ospedale Civico di Lugano, Neurocenter of Italian Switzerland, Via Tesserete 46, 6900 Lugano, Switzerland. Email: anna.castelnovo@eoc.ch.
†These authors contributed equally to this work.

Abstract

Study Objectives: The umbrella term "Disorders of Arousal" (DoA), encompassing sleepwalking, confusional arousals, and sleep terrors, refers to parasomnias manifesting during nonrapid eye movement (NREM) sleep, commonly thought to arise from an aberrant arousal process. While previous studies have detailed electroencephalographic (EEG) changes linked to DoA episodes, it remains uncertain how these alterations differ from a physiological arousal process. This study directly compared brain activity between DoA episodes and arousals associated with physiological movements (motor arousal) in individuals with DoA and healthy sleepers.

Methods: Fifty-three adult participants with DoA (25 males, 32.2 ± 15.5 years) and 33 control participants (14 males, 31.4 ± 11.4 years) underwent one or more home EEG recordings. A semiparametric regression model was employed to elucidate the complex relationship between EEG activity across channels, within and across different groups, including motor arousals in DoA (n = 169), parasomnia episodes in DoA (n = 361), and motor arousals in healthy sleepers (n = 137).

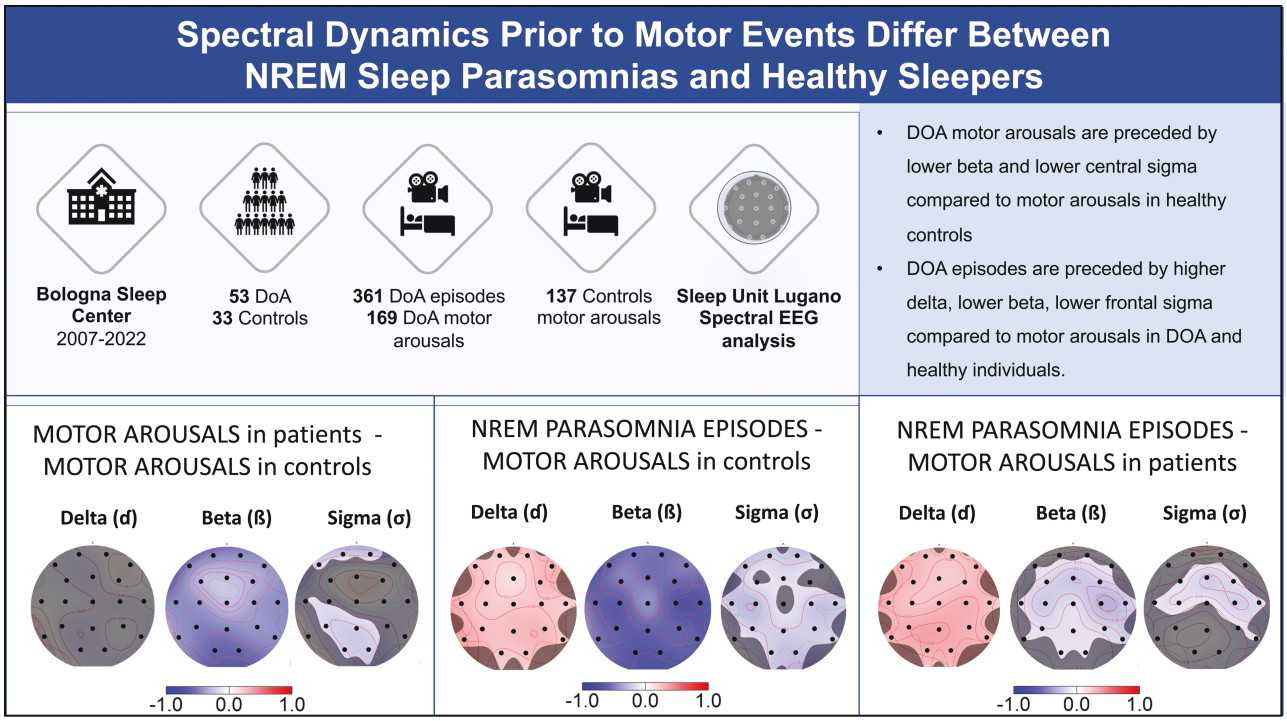
Results: Parasomnia episodes and motor arousals in both groups were preceded by a diffuse increase in slow-wave activity (SWA) and beta power, and a widespread decrease in sigma power. However, motor arousals in DoA displayed lower beta and central sigma than in healthy sleepers. Within participants with DoA, episodes were preceded by lower beta, frontal sigma, and higher SWA than motor arousals.

Conclusions: Our findings suggest that the arousal process is altered in participants with DoA, and that specific EEG patterns are required for DoA episodes to emerge. These insights will help guide future research into the underlying circuits and objective markers of DoA.

Key words: NREM parasomnias; somnambulism; electroencephalography; topography; sleep spindles

Submitted for publication: July 20, 2024; **Revised:** October 21, 2024

Graphical Abstract



Statement of Significance

Our findings identify specific brain abnormalities associated with the arousal process in participants with nonrapid eye movement (NREM) parasomnias compared to healthy sleepers. While a stable, intrinsic difference in the arousal process may predispose affected participants to exhibit complex motor behaviors during sleep, additional changes in regional brain activity patterns are necessary for an arousal response to progress into a clinical NREM parasomnia episode. These results are a crucial step toward understanding the brain mechanisms underlying NREM parasomnias and pave the way for future studies to identify objective markers for these disorders.

Introduction

Confusional arousal, sleep terrors, and sleepwalking, collectively known as disorders of arousal (DoA), are relatively common conditions in the general population [1], falling under the category of nonrapid eye movement sleep (NREM) parasomnias [2]. This family of disorders is characterized by recurrent undesired complex behaviors performed in a state of absence or inadequate responsiveness, coupled with inappropriate judgment abilities arising out NREM sleep [3, 4]. During these episodes, affected participants can involuntarily endanger themselves and others, with some cases even involving DoA-related pseudo-suicide and homicide [5–7]. Clinical management of these phenomena is challenging due to the limited understanding of their pathophysiology. Growing evidence suggests that these behavioral states reflect the emergence of local wake-like electroencephalographic (EEG) activity within specific (mainly motor and limbic) brain regions during NREM sleep [8–13]. The abnormal coexistence of wake-like and sleep-like EEG patterns during DoA episodes has been interpreted in the context of an abnormal arousal process, hence the name "DoA" [5].

Over the last two decades, EEG studies targeting individuals with DoA aimed to characterize the neurophysiologic activity preceding DoA episodes through visual, spectral power, or connectivity analysis [14]. Most studies focused on delta/slow-wave activity (SWA), particularly on fronto-central leads. A common finding across these studies is an increase in delta power, especially in frontal areas, in the seconds immediately preceding an episode, with variability in the chosen time window. Recently, we performed a systematic spectral analysis on 325 DoA episodes (from 103 consecutive video-polysomnographic recordings of 53 adult participants with DoA), showing a significant increase in all frequency bands preceding DoA episodes, excluding sigma, which displayed the opposite effect [15].

An essential question that remains unanswered is the extent to which these EEG changes before behavioral episodes are unique to NREM parasomnias or if they are intrinsic to the normal arousal process. Siclari et al. conducted a high-density EEG analysis on both normal awakenings ($n = 25$) and parasomnia episodes ($n = 96$, 59 spontaneous, 37 provoked by sleep deprivation alone or associated with sounds) from 17 participants with DoA[16]. Compared to normal awakenings, parasomnia episodes displayed higher SWA (1–4 Hz) up to 1 minute prior to the event and lower beta activity over the entire scalp, with no specific regional pattern. However, this study lacked healthy control participants, leaving uncertainty about intrinsic alterations of the arousal process in participants with DoA.

Only one case report [17] and a small EEG study [18] compared parasomnia episodes with healthy control participants. Zadra and Nilsen observed higher SWA (0.75–3.75 Hz) over fronto-central regions (left > right) during the minute preceding the onset of three sleep terrors compared to 1-minute segments extracted from slow-wave sleep (SWS) in 10 control participants. Espa et al. conducted a comparison between a 2-minute window preceding behavioral and nonbehavioral arousal out of NREM in 11 adult participants with DoA and 11 matched healthy control participants. Within the group of participants with DoA, they identified significantly higher mean SWA values before parasomnia episodes compared to "normal" arousals. However, no differences were observed between parasomnia participants and control groups in the 2-min window preceding normal arousals (150 vs. 40, respectively). This study is limited by a relatively small sample size, the relatively long-time window considered (as later studies identified specific changes in the last seconds prior to behavioral and nonbehavioral arousals), the absence of control for NREM sleep stage and cycles (known to affect SWA), event duration, and the random effect related to the different numbers of events across participants. Furthermore, frequencies above SWA were not explored.

With this study, we aimed to differentiate the EEG changes preceding parasomnia episodes from those inherent in the normal arousal process. To accomplish this objective, we conducted a thorough comparative analysis of EEG activity across the entire scalp immediately prior to 137 motor arousals in healthy controls, 169 motor arousals in individuals with DoA, and 361 DoA episodes.

Methods

This is a monocentric observational study that includes clinical sleep evaluations and at-home sleep recordings. The study received approval from the local Ethical Committee "Comitato Etico Interaziendale Bologna-Imola," CE-BI, code 17176/2017. All participants provided written informed consent in accordance with the Helsinki Convention.

Participants

All participants enrolled in the study were consecutively referred to the Sleep Center of the Department of Biomedical and NeuroMotor Sciences, University of Bologna, and IRCCS Istituto delle Scienze Neurologiche di Bologna, between 2007 and 2021. They were evaluated by a sleep disorder specialist (FP). Inclusion criteria required a clinical diagnosis of DoA based on ICSD—III criteria [2], confirmed by video-polysomnography (VPSG) recording of at least one DoA episode. Exclusion criteria included neurological or psychiatric disorders, psychotropic therapy, and other sleep disorders. Clinical data, such as age, sex, family history of parasomnia, age of onset, and frequency of episodes at observation, were collected. This dataset entirely overlaps with the dataset described in Mainieri et al. [15] and has a significantly larger sample size than any other previous quantitative EEG study conducted on DoA.

In addition to participants with DoA, a convenience sample of 33 age- and sex-matched healthy controls were consecutively recruited from March 2018 to May 2022. Healthy participants were chosen through word of mouth or among caregivers/partners of participants at the Sleep Center. All control participants were screened by sleep disorder specialists (F.P.) and had the mandatory requisite of perceiving their own sleep as refreshing. Exclusion criteria for controls included past and present history of sleep disorders, relevant clinical/neurological and psychiatric conditions, and psychotropic therapy.

EEG data collection

Control participants underwent a single nocturnal home-VPSG, while participants underwent at least two nocturnal home-VPSGs using XLTEK Trex HD (Natus Medical Incorporated) and a video camera (Handycam HDR-CX700, Sony, 12.3 Megapixel resolution). Participants were instructed to maintain their habitual sleep routine in the week preceding the exam. All recordings were performed using a 32-channel VPSG system with vertex referencing and digitized at a sampling rate of 256 Hz. VPSG recordings included standard bipolar EEG (International 10-20 system) with 19 electrodes (Fp1, Fp2, F3, F4, F7, F8, Fz, C3, C4, Cz, T3, T4, T5, T6, P3, P4, Pz, O1, and O2), electrocardiogram, electrooculogram, chin and both anterior tibialis electromyography (EMG), thoracoabdominal plethysmography bands, and synchronized audio-video recording. The recordings utilized a DC filter to eliminate drift and slow components. Sleep stages were scored in 30-second epochs according to AASM criteria [19] using the Natus ® NeuroWorks EEG Software. In the rare cases, where technical issues were recorded in the vPSG recordings, these were repeated, so there are no missing data.

Visual identification of motor arousals and episodes

All full-night VPSG recordings underwent independent review by two sleep specialists (G.M., G.L.) to assess the overall recording quality, including artifacts, technical issues, and the presence of disturbing noises or lights. Specifically, events with clear visibility on the video recordings were included for the study's analysis. DoA episodes were scored according to three specific patterns of increasing complexity [20]. In cases where discrepancies arose between the two observers regarding the classification of DoA episodes, a third observer, a sleep specialist with expertise in the semiology of nocturnal motor episodes (FP), resolved any disagreements.

In the pool of participants with DoA and healthy controls, motor arousals were defined as those associated with physiological movements, including body position changes, adjusting posture, scratching, stretching, and arranging dresses or blankets [21]. To compare with the minority of DoA episodes arising from the NREM stage 2, a corresponding number of motor arousals from the NREM stage 2 stage were marked. Visible arousals at the EEG not associated with major movements were excluded from this study.

The beginning of each event (either an episode or a motor arousal) was time-marked with either the first EMG activation or the first visible movement (including eye opening) on the video analysis. The end of each event was determined as the last visible movement on the video review (including eye opening). The collected features for each event included the emerging sleep stage, the sleep cycle, and the duration. In instances where sleep staging within the 3 minutes preceding a given event was not stable (an admixture of NREM stages 3 and 2), a mixed sleep stage 2.5 variable was created. Sleep cycles beyond the third sleep cycle were grouped together into a single variable. Duration was defined as the time in seconds between the beginning and the end of each motor event.

EEG analysis

The data were converted into a European Data Format file and subsequently imported into MATLAB (MathWorks Inc., Natick,

MA, 2020a). For each episode, 6-minute segments preceding the onset were extracted. These segments underwent visual inspection aided by a user graphical interface (https://github.com/CSC-UW/csc-eeg-tools) to identify noisy channels and epochs.

Additional spectral-based and topographic procedures were employed to detect individual channels with significantly greater power compared to neighboring channels or epochs displaying deviant spectra or topographies. Each segment was then subjected to band-pass filtering (zero-phase digital low-pass and high-pass filter with reflection, 0.5–45 Hz, using the "filtfilt" function of the signal-processing toolbox). Channels marked as bad were interpolated using spherical interpolation, while epochs marked as bad were discarded.

The filtered signal was re-referenced to the average scalp voltage and divided into consecutive 5-second epochs. Spectral analysis was performed on clean 5-s epochs, covering a total of 360 s preceding each episode, using the Fast Fourier Transform (Welch-averaged modified periodogram with a Hamming window, 50% overlap). For topographic analysis, spectral density was averaged in six frequency ranges (SWA or delta: 0.5–4 Hz; theta: 4–8 Hz; alpha: 8–12 Hz; sigma: 12–15 Hz; beta: 15–25 Hz; and low gamma: 25–45 Hz). The primary focus was on delta and sigma bands, which are known to reflect the activity of NREM slow waves and sleep spindles. Beta band was also analyzed as representative of high EEG frequencies.

For this study, we extracted the 5-second time window before each event (whether it be a DoA episode or a physiological movement in either the DoA or control group), referred to as the "pre-event" time. Additionally, we considered the time frame of 60 seconds spanning from 2 to 3 minutes before each event, denoted as the "baseline" period, which represents stable sleep without any motor arousal or microarousal.

Statistical analysis

All recordings, including multiple sleep sessions from individual participants, were included in the current analyses. To explore changes in voltages measured by different electrodes over time among different groups (DoA vs. control) and conditions (DoA episodes and motor arousals), we utilized a generalized additive mixed model (GAMM) [22]. GAMM is a nonlinear regression technique that extends general linear mixed models to accommodate nonlinear dependencies between response and predictor variables. This is achieved by incorporating a set of smooth functions. GAMMs are characterized by high flexibility in handling complex data with possibly nonlinear spatiotemporal relationships. They allow for the inclusion of fixed and random effects, as well as smooth terms.

We specifically modeled activity in delta, sigma, and beta bands, treating subject ID and night of recording as random effects. Additionally, we incorporated a nonlinear interaction term to address potential differential activity across spatial electrode coordinates for each group.

In our model, fixed effects included sex, age, sleep cycle, time of motor event from sleep onset, and event duration, as these variables are known to impact power spectral density. Furthermore, we introduced a grouping variable formed by the interaction between a group–condition variable with three time-dependent categories (DoA episodes, DoA movements, control movements) and a time variable with two values, T0 (baseline measurements, taken three to two minutes before the first movement onset) and T1 (measurements five seconds prior to movements/episodes onset). This approach facilitates direct comparisons between groups and time, with participants exhibiting DoA movements at T0 chosen as the reference group.

Throughout the model, the outcome variable is represented by standardized activity (Z-scores) in each band, transformed to meet underlying model assumptions. We utilized the ordered quantile normalization transformation, a rank-based procedure that maps percentiles of the original values to those of the normal distribution.

Additionally, we introduced a nonlinear interaction term between 2D electrode coordinates, allowing variation for each level of the interaction group–condition–time. To enhance interpretation, fitted values from the models are visualized using topographic maps.

Results

Sample of participants, motor arousals, and DoA episodes

We considered a total of 33 healthy controls (14 males, mean age 31.4 ± 11.4 years) and 53 participants with DoA (25 males, mean age 32.2 ± 15.5 years years) for power spectral analyses. Overall, we analyzed 137 motor arousals in healthy controls, 169 motor arousals in DoA, and 361 DoA episodes. Clinical DoA features and sleep macro-architectural data for both participants and controls are summarized in Supplementary Tables 1 and 2. The main findings on delta, sigma, and beta are reported below, while additional exploratory analyses of other frequency bands are summarized in Supplementary Figures 1 and 2.

Model summary results for the delta band

Random effects and fixed effects of GAMM model covariates in the delta band are presented in Table 1. Model checking plots are shown in Supplementary Figure 3.

Sleep cycles showed a significant negative effect, resulting in lower power spectral density in the delta band across cycles. Conversely, stages demonstrated a positive effect, with higher power spectral density in the delta band observed in stage 3 compared to stage 2. The event duration exhibited a significant positive effect, indicating higher delta power for longer events. Model results are adjusted for age and gender, which were included as fixed covariates. Notably, within each group, a significant positive difference was found between pre-event activity and baseline delta activity, meaning that delta power increased from baseline to pre-event (Figure 1). This effect involved the entire scalp surface. Of note, an exploratory analysis conducted on high (2–4 Hz) and low (0.5–2 Hz) delta revealed an opposite trend: a decrease in high delta from baseline to pre-event and an increase in low delta from baseline to pre-event (data not shown) in all groups. This finding aligns with the known increase in high-voltage large K-complexes (or Type I slow waves) prior to motor events, compared to smaller (Type II) slow waves [16]. Furthermore, there was a significant (positive) difference between the DoA pre-episode and premotor arousal period and between the DoA pre-episode and the premotor arousal period in control participants (Figure 2). Again, this effect was observed across the entire scalp surface. No difference could be detected between motor arousals in DoA and motor arousals in healthy control participants (Figure 2). Similar between-group effects were observed for both high and low delta (data not shown).

Model summary results for the sigma band

Random and fixed effects of covariates included in the GAMM model in the sigma band are presented in Table 2. Model checking plots are shown in Supplementary Figure 4.

Table 1. Estimated GAMM model for delta band

A. Parametric coefficients	**Estimate**	**Std. error**	***P*-value**
Intercept	−1.1458	0.3300	.0005
Sex (male vs. female)	0.3769	0.0395	<.0001
Age	0.0076	0.0017	<.0001
Interaction (ref.=T0.DoA.m)			
T1.DoA.m	0.3618	0.0254	<.0001
T0.DoA.e	0.2735	0.0238	<.0001
T1.DoA.e	0.6548	0.0241	<.0001
T0.HC.m	0.0330	0.0453	.4658
T1.HC.m	0.3989	0.0458	<.0001
Duration	0.0009	0.0001	<.0001
Cycle (ref = 1)			
2	−0.0406	0.0099	<.0001
3	−0.1058	0.0118	<.0001
4	−0.1786	0.0159	<.0001
Stage (ref. = 2)			
2.5	0.4258	0.0177	<.0001
3	0.9093	0.0142	<.0001
B. Smooth terms	**edf**	**Ref.df**	***P*-value**
s(ID)	78.5706	80	<.0001
s(oNIGHT12)	4.9918	5	<.0001
te(X,Y):Interaction_T0.DoA.m	17.2813	17.9368	<.0001
te(X,Y):Interaction_T1.DoA.m	17.3641	17.9501	<.0001
te(X,Y):Interaction_T0.DoA.e	17.6477	17.9844	<.0001
te(X,Y):Interaction_T1.DoA.e	17.678	17.9869	<.0001
te(X,Y):Interaction_T0.HC.m	16.9507	17.867	<.0001
te(X,Y):Interaction_T1.HC.m	17.1969	17.9215	<.0001
Post hoc analysis			
Contrast	**Estimate**	***SE***	***P*-value**
T1–T0 (DoA.m)	0.34	0.06	<.0001
T1–T0 (DoA.e)	0.37	0.04	<.0001
T1–T0 (HC.m)	0.37	0.07	<.0001

The variable GROUP_COND has three time-dependent categories: DoA.m (motor arousal in DoA), DoA.e (DoA episodes), and HC.m (motor arousal in healthy control subjects). This variable combines the original information on GROUP (DoA or healthy control) with CONDITION ("m" for motor arousal or "e" for DoA episode). The variable "Interaction" represents the interaction between GROUP, CONDITION, and TIME, which take two values: T0 (for baseline measurements taken from 3 to 2 minutes before "m" or "e" motor onset) and T1 (for measurements taken 5 seconds prior to "m" or "e" motor onset). Post hoc multiple pairwise comparisons between levels of the GROUP_COND variable after the GAMM model are also reported.

Sleep cycles showed a significant effect, resulting in lower power spectral density in the sigma band across cycles. Furthermore, a negative effect was estimated for stages, with lower power spectral density in the sigma band observed in stage 3 compared to stage 2. Model results are adjusted for age and gender, which were included as fixed covariates. Notably, within each group, a significant negative difference was found between pre-event activity and baseline sigma activity, meaning that sigma power decreased from baseline to pre-event (Figure 1). This effect mainly involved central brain regions for motor arousals in both groups (DoA and control). Furthermore, a significant negative difference was estimated between the DoA pre-episode and the DoA premotor arousal period over frontal brain regions, indicating that DoA episodes were preceded by lower frontal sigma compared to DoA movements (Figure 2). Additionally, a significant negative difference was found between the DoA premotor arousal period and the control premotor arousal period over central-posterior brain regions, meaning that DoA movements were preceded by lower central sigma compared to movements in control participants (Figure 2). Lastly, a significant negative difference was identified between the DoA pre-episode and the premotor arousal period in control participants (Figure 2), which was rather diffuse across scalp electrodes. In simpler terms, sigma power was globally lower prior to DoA episodes compared to motor arousals in healthy control participants.

Model summary results for the beta band

Random effects and fixed effects of cofactors under GAMM in the beta band are presented in Table 3. Model checking plots are shown in Supplementary Figure 5.

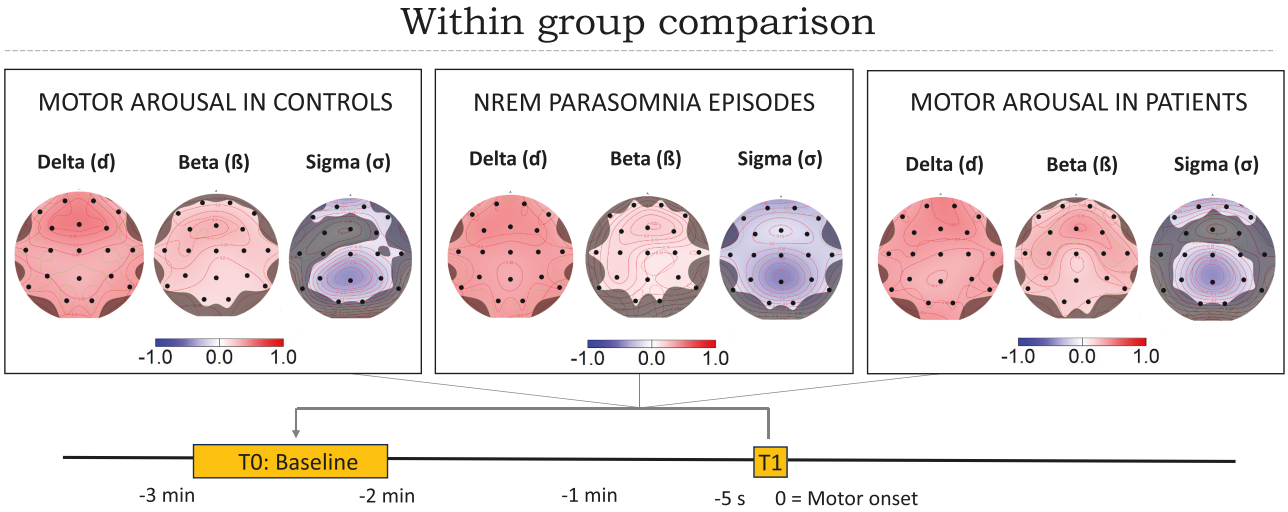


Figure 1. Within-group contrasts for EEG delta (1–4 Hz), sigma (11–15 Hz), and beta activity (15–25 Hz). The maps illustrate the estimated spatial differences between T0 and T1 (left) and their corresponding significance regions (right) across different groups. Red color indicates positive difference in EEG activity and in particular higher EEG activity in the second group compared to the first group in each panel, while gray represents nonsignificant areas. (Left) Pre-event versus baseline in the control group (center) pre-event (episodes) versus baseline in the DoA group. (Right) Pre-event (motor arousals) versus baseline in the DoA group. The maps depict the estimated surfaces (fitted values) at T0 and T1 across different groups.

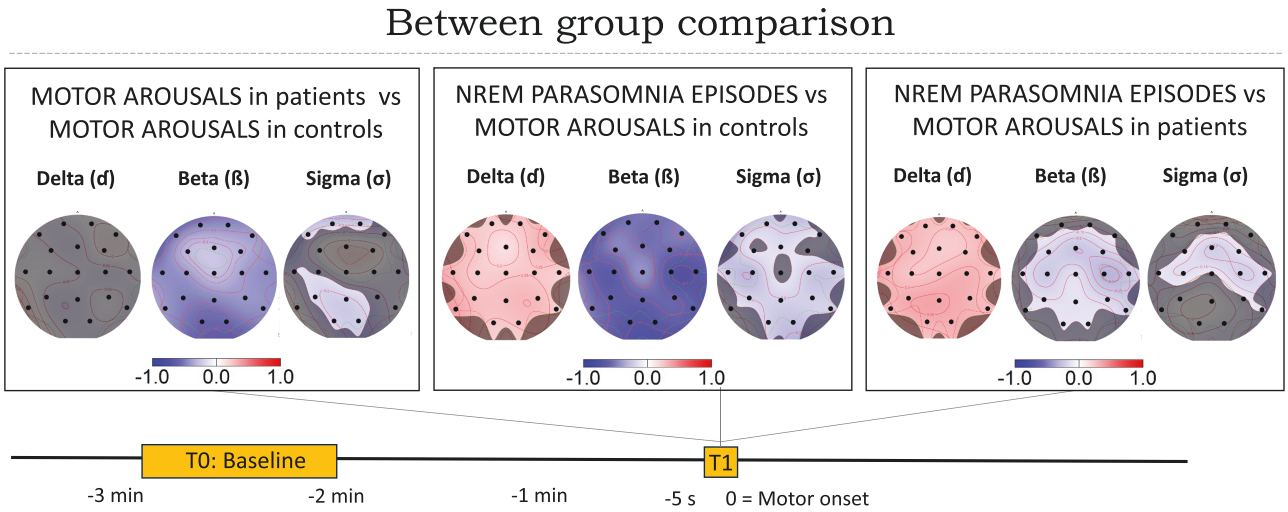


Figure 2. Between-group contrasts for EEG delta (1–4 Hz), sigma (11–15 Hz), and beta activity (15–25 Hz). The maps illustrate the estimated surfaces (fitted values) at pre-event for episodes and motor arousals in the DoA group and for motor arousals in control subjects. Higher values are shown in red and lower in blue. The lower maps display the estimated spatial differences between groups and their corresponding significance regions (right) across different groups. Red color indicates positive difference in EEG activity and in particular higher EEG activity in the second group compared to the first group in each panel, while gray represents nonsignificant areas. (Left) DoA pre-event (motor arousals) vs control pre-event (motor arousals). (Center) DoA pre-event (episodes) vs control pre-event (motor arousals). (Right) DoA pre-event (episodes) vs DoA pre-event (motor arousals).

Age did not emerge as a significant predictor of activity in the beta band. A significant positive effect was observed for gender, indicating that males exhibited higher beta power than females. Sleep cycles showed a significant effect, resulting in lower power spectral density in the beta band across cycles. Stages demonstrated a negative effect, with lower power spectral density in the beta band observed in stage 3 compared to stage 2. The event duration exhibited a significant negative effect, indicating lower beta power for longer events. Notably, within each group, a significant positive difference was found between pre-event activity and baseline beta activity, meaning that beta power increased from baseline to pre-event (Figure 1). This effect was observed across the entire scalp surface. Furthermore, there was a significant negative difference between the DoA pre-episode and premotor arousal period in DoA (Figure 2), between the DoA premotor episode and the premotor arousal period in control participants (Figure 2), and between motor arousals in DoA and motor arousals in healthy control participants (Figure 2). In other words, DoA episodes were preceded by lower beta activity compared to both motor arousals in DoA and motor arousals in healthy sleepers, and motor arousal by lower beta activity in participants compared to controls.

Discussion

In this study, we examined the EEG spectral activity preceding over 300 episodes of DoA and over 300 arousals associated with physiological body movements in a large sample of both adult participants with DoA ($n = 53$) and healthy participants ($n = 33$).

Table 2. Estimated GAMM model for sigma band

A. Parametric coefficients	Estimate	Std. error	P-value
Intercept	0.6517	0.4139	.1154
Sex (male vs. female)	0.5223	0.0413	<.0001
Age	−0.0068	0.0018	.0001
Interaction (ref.=T0.DoA.m)			
T1.DoA.m	−0.1554	0.0231	<.0001
T0.DoA.e	−0.0128	0.0231	.5805
T1.DoA.e	−0.2504	0.0225	<.0001
T0.HC.m	0.1050	0.0466	.0244
T1.HC.m	−0.0495	0.0459	.2806
Duration	−0.0002	0.0001	.0414
Cycle (ref = 1)			
2	−0.159	0.0104	<.0001
3	−0.1932	0.0124	<.0001
4	−0.2237	0.0167	<.0001
Stage (ref.=2)			
2.5	−0.0546	0.0186	.0033
3	−0.2716	0.0149	<.0001
B. Smooth terms	**edf**	**Ref.df**	**P-value**
s(ID)	78.4942	80	<.0001
s(oNIGHT12)	4.9945	5	<.0001
te(X,Y):Interaction_T0.DoA.m	16.9002	17.8507	<.0001
te(X,Y):Interaction_T1.DoA.m	16.6354	17.781	<.0001
te(X,Y):Interaction_T0.DoA.e	17.5752	17.9774	<.0001
te(X,Y):Interaction_T1.DoA.e	17.481	17.9665	<.0001
te(X,Y):Interaction_T0.HC.m	16.858	17.8438	<.0001
te(X,Y):Interaction_T1.HC.m	16.0518	17.5673	<.0001
Post hoc analysis			
Contrast	**Estimate**	**SE**	**P-value**
T1–T0 (DoA.m)	−0.31	0.07	<.0001
T1–T0 (DoA.e)	−0.33	0.05	<.0001
T1–T0 (HC.m)	−0.26	0.07	<.0001

The variable GROUP_COND has three time-dependent categories: DoA.m (motor arousal in DoA), DOA.e (DoA episodes), and HC.m (motor arousal in healthy control subjects). This variable combines the original information on GROUP (DoA or healthy control) with CONDITION ("m" for motor arousal or "e" for DoA episode). The variable "Interaction" represents the interaction between GROUP, CONDITION, and TIME, which takes two values: T0 (for baseline measurements taken from 3 to 2 minutes before "m" or "e" motor onset) and T1 (for measurements taken 5 seconds prior to "m" or "e" motor onset). Post hoc multiple pairwise comparisons between levels of the GROUP_COND variable after the GAMM model are also reported.

Motor arousal in healthy participants

The power spectral distribution preceding motor arousals in healthy control participants exhibited an increase in delta and beta band frequencies and a decrease in sigma band frequencies, aligning perfectly with the current available literature.

The sigma band is inherently suppressed during cortical arousal, as defined by the Academy of Sleep Medicine [19], and demonstrated in both scalp and stereo-EEG studies [23, 24]. Moreover, cortical arousal is known to more likely occur during NREM sleep phases characterized by low sigma power [25] and heightened locus coeruleus activity during NREM sleep [26].

The decrease in the sigma band preceding an arousal is generally accompanied by increased SWA, primarily in the form of a K-complex [23]. These K-complexes are typically more pronounced in the parietal and frontal cortices [27] and when associated with a microarousal, they are linked to an elevation in beta band power, particularly in the motor cortex [27].

In general, prior studies have observed an elevation and coexistence of slow (delta, theta) and fast (alpha, beta) scalp EEG frequencies in the seconds directly preceding arousal [28], whether spontaneous or associated with periodic limb movements [29, 30]. This mixed activity has been described even in the absence of a noticeable motor arousal, as recurring local activations in the motor cortex, characterized by a prominent alpha and/or beta rhythm, co-occur with a simultaneous increase in slow waves in frontal brain regions [31].

Motor arousal in participants with DoA

Motor arousal (in the absence of clinical events) in participants with DoA compared to healthy control participants was preceded

Table 3. Estimated GAMM model for beta band

A. Parametric coefficients	Estimate	Std. error	P-value
Intercept	0.2371	0.3878	.5409
Sex (male vs. female)	0.5062	0.0403	<.0001
Age	0.0006	0.0017	.7498
Interaction (ref.=T0.DoA.m)			
T1.DoA.m	0.2617	0.0217	<.0001
T0.DoA.e	–0.0341	0.0215	.113
T1.DoA.e	0.0989	0.0214	<.0001
T0.HC.m	0.4695	0.0445	<.0001
T1.HC.m	0.6841	0.0444	<.0001
Duration	–0.0003	0.0001	<.0001
Cycle (ref = 1)			
2	–0.2114	0.0101	<.0001
3	–0.2778	0.0119	<.0001
4	–0.2886	0.0161	<.0001
Stage (ref.=2)			
2.5	–0.0747	0.0179	<.0001
3	–0.4454	0.0144	<.0001
B. Smooth terms	**edf**	**Ref.df**	**P-value**
s(ID)	78.6528	80	<.0001
s(oNIGHT12)	4.994	5	<.0001
te(X,Y):Interaction_T0.DoA.m	16.8615	17.8439	<.0001
te(X,Y):Interaction_T1.DoA.m	16.4328	17.715	<.0001
te(X,Y):Interaction_T0.DoA.e	17.4811	17.9661	<.0001
te(X,Y):Interaction_T1.DoA.e	17.4677	17.9647	<.0001
te(X,Y):Interaction_T0.HC.m	16.0213	17.5567	<.0001
te(X,Y):Interaction_T1.HC.m	15.7046	17.4155	<.0001
Post hoc analysis			
Contrast	**Estimate**	**SE**	**P-value**
T1–T0 (DoA.m)	0.21	0.06	<.0001
T1–T0 (DoA.e)	0.13	0.04	<.0001
T1–T0 (HC.m)	0.22	0.07	<.0001

The variable GROUP_COND has three time-dependent categories: DOA.m (motor arousal in DoA), DOA.e (DoA episodes), and HC.m (motor arousal in healthy control subjects). This variable combines the original information on GROUP (DoA or healthy control) with CONDITION ("m" for motor arousal or "e" for DoA episode). The variable "Interaction" represents the interaction between GROUP, CONDITION, and TIME, which take two values: T0 (for baseline measurements taken from 3 to 2 minutes before "m" or "e" motor onset) and T1 (for measurements taken 5 seconds prior to "m" or "e" motor onset). Post hoc multiple pairwise comparisons between levels of the GROUP_COND variable after the GAMM model are also reported.

by lower beta and sigma power, in the presence of similar SWA levels. While confirming the preliminary findings by Espa et al. regarding delta power [18], our results pinpoint that motor arousal in DoA tends to occur against a distinct EEG background compared to healthy control participants.

Specifically, lower sigma power over centro-parietal brain regions suggests reduced levels of fast sleep spindles, which may imply a potential reduction in mechanisms that safeguard sleep continuity. Indeed, sleep spindles play a crucial role in inhibiting sensory activation of the cortex, contributing significantly to decreased sensory responsiveness during sleep [32, 33]. As a consequence, a decline or low occurrence of spindles constitutes a vulnerability period, during which we are more prone to waking up in response to sensory stimulation [25].

At the same time, decreased beta activity may suggest a less "activated" state marked by lower levels of cortical arousal. Notably, beta/gamma frequencies are linked to the processing of sensory information during active wakefulness [34]. Intriguingly, EEG quantitative studies in participants with insomnia have reported heightened beta activity before sleep onset and during sleep, correlating with increased arousal levels, consciousness, and mental activity during sleep [35–37].

Finally, reduced sigma and beta power preceding motor arousal in participants with DoA in the absence of SWA changes may suggest a possible disruption in the established reciprocal oscillation between sigma/beta and delta during sleep [38, 39].

When an arousal becomes an episode in participants with DoA?

Regardless of the presence of behavioral manifestations of parasomnia, NREM motor events in participants with DoA (either

episodes or simple arousals) were preceded by a pronounced increase in both delta and beta power, accompanied by a decrease in sigma power. This pattern closely resembles the spectrum observed before motor arousal in healthy control participants. Strikingly, longer events showed a more pronounced effect, indicating a connection between the sleep background at the onset of an arousal and its subsequent development.

Within participants with DoA, a regular motor arousal was more likely to occur when the sleep background was more "activated" (lower SWA, higher beta), facilitating the transition to wakefulness. Conversely, DoA episodes appeared to arise from a less activated EEG background, aligning with the findings of a recent high-density EEG study [16]. Cataldi et al. found higher SWA and lower beta 1 minute before DoA motor onset compared to DoA normal awakenings. Unexpectedly, this effect was stronger from –60 up to –10 seconds prior to motor onset, and the SWA effect disappeared just immediately prior to motor onset. Unlike the aforementioned study, our research revealed significant differences in the delta band immediately before motor onset. The fact that EEG changes become detectable only 5–6 seconds prior to motor onset is supported by other scalp EEG studies [40–43], and more notably, by a stereo-EEG study [9]. This disparity may be attributed to the larger sample size, a distinct cleaning procedure (visual versus Artifact Subspace Reconstruction automatic cleaning), and a statistical model that also accounted for stages and time from sleep onset. Furthermore, we expanded our analysis to the sigma band, disclosing a diminished level of frontal sigma activity in the moments preceding DoA episodes compared to DoA motor arousals. When comparing DoA episodes to motor arousal in healthy participants, a similar EEG pattern could be observed in DoA, characterized by higher SWA and lower beta/sigma activity. However, sigma activity was lower in both frontal and parietal brain regions.

Remarkably, two independent studies proposed a "trait-like" reduction in sleep spindle density—unrelated to any signs of arousal—specifically during SWS in individuals with DoA when compared to controls [18, 44]. Unfortunately, these studies did not characterize sleep spindle topography and mean frequency, preventing conclusive statements regarding sleep spindle subtypes, neither investigated their relationship with motor events.

Collectively, the current findings suggest that motor events in DoA (either episodes or motor arousals) tend to emerge from an EEG with fewer central sleep spindles compared to healthy participants and with widespread lower beta. Additionally, the likelihood of arousal transitioning to a DoA episode increases when frontal sleep spindles are also abnormally low and SWA is higher. In other words, DoA episodes seem to emerge in the context of a decoupling between higher arousability levels (as reflected by lower sigma) and a less activated cortical background (higher SWA, lower beta). To better understand the specificity and significance of current findings, it will be crucial to compare EEG activity changes observed in DoA episodes and DoA arousals with those in other sleep disorders, characterized by abnormal movements/events during sleep. Specifically, future studies must investigate the potential use of these findings in the differential diagnosis of sleep-related hypermotor epilepsy (SHE), especially in the presence of minor events that are often otherwise indistinguishable. Additionally, identifying specific patterns preceding DoA episodes could open the way to identifying time windows when episodes are easier to trigger in a laboratory setting. This would not only advance research on these disorders but also improve the diagnostic process.

Limitations and Future Directions

While our study provides valuable insights into the EEG activity preceding parasomnia episodes and motor arousals, it is crucial to acknowledge certain limitations. One notable constraint is the absence of high-density EEG (hd-EEG) data in our investigation. Hd-EEG, which utilizes a larger number of electrodes, offers superior spatial resolution to provide a more detailed and accurate representation of neural activity and allows to effectively manage noise contamination. Future research endeavors employing hd-EEG could offer a more comprehensive understanding of the intricate EEG dynamics during parasomnia episodes.

Notably, our study focused on adult populations, constituting a minority albeit a more severely affected subgroup of participants with DoA. Consequently, we could not disentangle between intrinsic effects and those arising from the chronic nature of the disorder. Although our findings are based on an adult cohort, the fundamental differences observed compared to baseline may suggest that similar patterns could be present in children. Future investigations should determine whether the results of our study can be generalized to younger age groups and delve into potential similarities and differences in brain activity between childhood and adulthood DoA, shedding light on the nuanced aspects of this condition across different age groups. Additionally, it is important to note that, based on previous studies, we limited our analyses to the 5-second window preceding motor onset. Future research should explore the temporal fluctuations of spectral dynamics in participants with DoA in relation to motor events and arousals over a broader time frame. Previous studies on the cyclic alternating pattern (CAP), a scoring system for transient EEG activations during NREM sleep that reflects arousal fluctuations, have shown that CAP rate—especially its slower component (CAP A1 phases)—is increased in participants with DoA, particularly during slow-wave sleep [45–47]. Investigating the relationship between CAP, spectral oscillations, and the occurrence of motor arousals or parasomnia episodes would be highly valuable.

Finally, further efforts are needed to better characterize EEG dynamics during parasomnia episodes in larger samples of participants. This will enhance our understanding of the underlying mechanisms and improve the diagnostic and therapeutic approaches for DoA.

Conclusions

In conclusion, this study delved into the intricate interplay between EEG frequencies and patterns preceding motor arousals and parasomnia episodes in both healthy individuals and those with DoA. Notably, irrespective of behavioral manifestations, NREM motor arousal in participants with DoA mirrors the EEG spectrum observed in healthy controls. Nevertheless, the arousal process itself appears altered in participants with DoA, emerging during periods of lower beta and sigma activity. In this context, DoA episodes only develop when frontal lobes are less activated but at the same time more arousable, displaying higher SWA and lower frontal sigma activity.

To sum up, this study sheds light on distinct EEG activity patterns associated with motor arousal in both groups, revealing a decoupling between frontal/central sigma, beta, and delta activity in participants with DoA, potentially compromising safeguards for sleep continuity.

Supplementary material

Supplementary material is available at *SLEEP* online.

Funding

A.C. was supported by the EOC Young Researchers Grant 2023. F.P. is supported by funding obtained under the National Recovery and Resilience Plan, Mission 4 Component 2 Investment 1.3—Call for tender No. 341 of 15/03/2022 of Italian Ministry of University and Research funded by the European Union—NextGenerationEU, Project code PE0000006, Concession Decree No. 1553 of 11/10/2022 adopted by the Italian Ministry of University and Research, CUP D93C22000930002, "A multi-scale integrated approach to the study of the nervous system in health and disease" (MNESYS). The publication of this article was supported by the "Ricerca Corrente 2023-2024" funding from the Italian Ministry of Health.

Conflicts of interest

None declared.

Data availability

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

References

1. Stallman HM, Kohler M. Prevalence of sleepwalking: a systematic review and meta-analysis. *PLoS One*. 2016;**11**(11):e0164769. doi:10.1371/journal.pone.0164769
2. American Academy of Sleep Medicine (AASM). *International Classification of Sleep Disorders (ICSD-3)*. 3rd ed. Darien, IL: American Academy of Sleep Medicine; 2014.
3. Zadra A, Desautels A, Petit D, Montplaisir J. Somnambulism: clinical aspects and pathophysiological hypotheses. *Lancet Neurol*. 2013;**12**(3):285–294. doi:10.1016/S1474-4422(12)70322-8
4. Mainieri G, Loddo G, Provini F, Nobili L, Manconi M, Castelnovo A. Diagnosis and management of NREM sleep parasomnias in children and adults. *Diagnostics (Basel)*. 2023;**13**(7):1261. doi:10.3390/diagnostics13071261
5. Castelnovo A, Lopez R, Proserpio P, Nobili L, Dauvilliers Y. NREM sleep parasomnias as disorders of sleep-state dissociation. *Nat Rev Neurol*. 2018;**14**(8):470–481. doi:10.1038/s41582-018-0030-y
6. Castelnovo A, Schraemli M, Schenck CH, Manconi M. The parasomnia defense in sleep-related homicide: a systematic review and a critical analysis of the medical literature. *Sleep Med Rev*. 2024;**74**:101898. doi:10.1016/j.smrv.2024.101898
7. Siclari F, Khatami R, Urbaniok F, *et al*. Violence in sleep. *Brain*. 2010;**133**(Pt 12):3494–3509. doi:10.1093/brain/awq296
8. Bassetti C, Vella S, Donati F, Wielepp P, Weder B. SPECT during sleepwalking. *Lancet*. 2000;**356**(9228):484–485. doi:10.1016/S0140-6736(00)02561-7
9. Terzaghi M, Sartori I, Tassi L, *et al*. Evidence of dissociated arousal states during nrem parasomnia from an intracerebral neurophysiological study. *Sleep*. 2009;**32**(3):409–412. doi:10.1093/sleep/32.3.409
10. Terzaghi M, Sartori I, Tassi L, *et al*. Dissociated local arousal states underlying essential clinical features of non-rapid eye movement arousal parasomnia: an intracerebral stereo-electroencephalographic study. *J Sleep Res*. 2012;**21**(5):502–506. doi:10.1111/j.1365-2869.2012.01003.x
11. Sarasso S, Pigorini A, Proserpio P, Gibbs SA, Massimini M, Nobili L. Fluid boundaries between wake and sleep: experimental evidence from Stereo-EEG recordings. *Arch Ital Biol*. 2014;**152**(2–3):169–177. doi:10.12871/0002982920142311
12. Flamand M, Boudet S, Lopes R, *et al*. Confusional arousals during non-rapid eye movement sleep: evidence from intracerebral recordings. *Sleep*. 2018;**41**(10). doi:10.1093/sleep/zsy139
13. Castelnovo A, Amacker J, Maiolo M, *et al*. High-density EEG power topography and connectivity during confusional arousal. *Cortex*. 2022;**155**:62–74. doi:10.1016/j.cortex.2022.05.021
14. Camaioni M, Scarpelli S, Gorgoni M, Alfonsi V, De Gennaro L. EEG patterns prior to motor activations of parasomnias: a systematic review. *Nat Sci Sleep*. 2021;**13**:713–728. doi:10.2147/NSS.S306614
15. Mainieri G, Loddo G, Castelnovo A, *et al*. EEG activation does not differ in simple and complex episodes of disorders of arousal: a spectral analysis study. *Nat Sci Sleep*. 2022;**14**:1097–1111. doi:10.2147/NSS.S360120
16. Cataldi J, Stephan AM, Marchi NA, Haba-Rubio J, Siclari F. Abnormal timing of slow wave synchronization processes in non-rapid eye movement sleep parasomnias. *Sleep*. 2022;**45**. doi:10.1093/SLEEP/ZSAC111
17. Zadra AL, Nielsenl TA. Topographical EEG mapping in a case of recurrent sleep terrors. *Dreaming*. 1998;**8**(2):67–74. doi:10.1023/B:DREM.0000005897.62698.1b
18. Espa F, Ondze B, Deglise P, Billiard M, Besset A. Sleep architecture, slow wave activity, and sleep spindles in adult patients with sleepwalking and sleep terrors. *Clin Neurophysiol*. 2000;**111**(5):929–939. doi:10.1016/s1388-2457(00)00249-2
19. Berry RB, Quan SF, Abreu AR. *The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications* (Version 3). American Academy of Sleep Medicine; 2023.
20. Loddo G, Sessagesimi E, Mignani F, *et al*. Specific motor patterns of arousal disorders in adults: a video-polysomnographic analysis of 184 episodes. *Sleep*. 2009;**41**(12). doi:10.1016/j.sleep.2017.08.019
21. Loddo G, Baldassarri L, Zenesini C, *et al*. Seizures with paroxysmal arousals in sleep-related hypermotor epilepsy (SHE): dissecting epilepsy from NREM parasomnias. *Epilepsia*. 2020;**61**(10):2194–2202. doi:10.1111/epi.16659
22. Wood SN. *Generalized additive models: an introduction with R*. Chapman and Hall/CRC; 2017.
23. Naitoh P, Antony-Baas V, Muzet A, Ehrhart J. Dynamic relation of sleep spindles and K-complexes to spontaneous phasic arousal in sleeping human subjects. *Sleep*. 1982;**5**:58–72. doi:10.1093/sleep/5.1.58
24. Peter-Derex L, Magnin M, Bastuji H. Heterogeneity of arousals in human sleep: a stereo-electroencephalographic study. *Neuroimage*. 2015;**123**:229–244. doi:10.1016/j.neuroimage.2015.07.057
25. Lecci S, Fernandez LMJ, Weber FD, *et al*. Coordinated infraslow neural and cardiac oscillations mark fragility and offline periods in mammalian sleep. *Sci Adv*. 2017;**3**(2):e1602026. doi:10.1126/sciadv.1602026
26. Osorio-Forero A, Cherrad N, Banterle L, Fernandez LMJ, Lüthi A. When the locus coeruleus speaks up in sleep: recent insights, emerging perspectives. *Int J Mol Sci* . 2022;**23**(9):5028. doi:10.3390/ijms23095028
27. Latreille V, von Ellenrieder N, Peter-Derex L, Dubeau F, Gotman J, Frauscher B. The human K-complex: Insights from combined

scalp-intracranial EEG recordings. *Neuroimage*. 2020;**213**:116748. doi:10.1016/j.neuroimage.2020.116748
28. Sforza E, Jouny C, Ibanez V. Cardiac activation during arousal in humans: further evidence for hierarchy in the arousal response. *Clin Neurophysiol*. 2000;**111**:1611–1619. doi:10.1016/s1388-2457(00)00363-1
29. Ferri R, Zucconi M, Rundo F, Spruyt K, Manconi M, Ferini-Strambi L. Heart rate and spectral EEG changes accompanying periodic and non-periodic leg movements during sleep. *Clin Neurophysiol*. 2007;**118**(2):438–448. doi:10.1016/j.clinph.2006.10.007
30. Ferrillo F, Beelke M, Canovaro P, *et al*. Changes in cerebral and autonomic activity heralding periodic limb movements in sleep. *Sleep Med*. 2004;**5**(4):407–412. doi:10.1016/j.sleep.2004.01.008
31. Nobili L, Ferrara M, Moroni F, *et al*. Dissociated wake-like and sleep-like electro-cortical activity during sleep. *Neuroimage*. 2011;**58**(2):612–619. doi:10.1016/j.neuroimage.2011.06.032
32. Fernandez LMJ, Lüthi A. Sleep spindles: mechanisms and functions. *Physiol Rev*. 2020;**100**(2):805–868. doi:10.1152/physrev.00042.2018
33. Dang-Vu TT, Bonjean M, Schabus M, *et al*. Interplay between spontaneous and induced brain activity during human non-rapid eye movement sleep. *Proc Natl Acad Sci USA*. 2011;**108**(37):15438–15443. doi:10.1073/pnas.1112503108
34. Grønli J, Rempe MJ, Clegern WC, Schmidt M, Wisor JP. Beta EEG reflects sensory processing in active wakefulness and homeostatic sleep drive in quiet wakefulness. *J Sleep Res*. 2016;**25**(3):257–268. doi:10.1111/jsr.12380
35. Li Y, Zou G, Shao Y, *et al*. Sleep discrepancy is associated with alterations in the salience network in patients with insomnia disorder: an EEG-fMRI study. *Neuroimage Clin*. 2022;**35**:103111. doi:10.1016/j.nicl.2022.103111
36. Baglioni C, Regen W, Teghen A, *et al*. Sleep changes in the disorder of insomnia: a meta-analysis of polysomnographic studies. *Sleep Med Rev*. 2014;**18**(3):195–213. doi:10.1016/j.smrv.2013.04.001
37. Stephan AM, Lecci S, Cataldi J, Siclari F. Conscious experiences and high-density EEG patterns predicting subjective sleep depth. *Curr Biol*. 2021;**31**(24):5487–5500.e3. doi:10.1016/j.cub.2021.10.012
38. Uchida S, Maloney T, Feinberg I. Beta (20-28 Hz) and delta (0.3-3 Hz) EEGs oscillate reciprocally across NREM and REM sleep. *Sleep*. 1992;**15**(4):352–358. doi:10.1093/sleep/15.4.352
39. Uchida S, Maloney T, March JD, Azari R, Feinberg I. Sigma (12–15 Hz) and delta (0.3–3 Hz) EEG oscillate reciprocally within NREM sleep. *Brain Res Bull*. 1991;**27**(1):93–96. doi:10.1016/0361-9230(91)90286-s
40. Januszko P, Niemcewicz S, Gajda T, *et al*. Sleepwalking episodes are preceded by arousal-related activation in the cingulate motor area: EEG current density imaging. *Clin Neurophysiol*. 2016;**127**(1):530–536. doi:10.1016/j.clinph.2015.01.014
41. Jaar O, Pilon M, Carrier J, Montplaisir J, Zadra A. Analysis of slow-wave activity and slow-wave oscillations prior to somnambulism. *Sleep*. 2010;**33**(11):1511–1516. doi:10.1093/sleep/33.11.1511
42. Guilleminault C, Poyares D, Abat F, Palombini L. Sleep and wakefulness in somnambulism: a spectral analysis study. *J Psychosom Res*. 2001;**51**:411–416. doi:10.1016/s0022-3999(01)00187-8
43. Desjardins ME, Carrier J, Lina JM, *et al*. EEG functional connectivity prior to sleepwalking: evidence of interplay between sleep and wakefulness. *Sleep*. 2017;**40**(4). doi:10.1093/sleep/zsx024
44. Carpentier N, O'Reilly C, Carrier J, *et al*. Spindles insufficiency in sleepwalkers' deep sleep. *Clin Neurophysiol*. 2020;**50**(5):339–343. doi:10.1016/j.neucli.2020.08.003
45. Zucconi M, Oldani A, Ferini-Strambi L, Smirne S. Arousal fluctuations in non-rapid eye movement parasomnias: the role of cyclic alternating pattern as a measure of sleep instability. *J Clin Neurophysiol*. 1995;**12**(2):147–154. doi:10.1097/00004691-199503000-00005
46. Bruni O, Ferri R, Novelli L, Finotti E, Miano S, Guilleminault C. NREM sleep instability in children with sleep terrors: the role of slow wave activity interruptions. *Clin Neurophysiol*. 2008;**119**(5):985–992. doi:10.1016/j.clinph.2008.01.015
47. Guilleminault C, Lee JH, Chan A, Lopes MC, Huang YS, da Rosa A. Non-REM-sleep instability in recurrent sleepwalking in prepubertal children. *Sleep Med*. 2005;**6**(6):515–521. doi:10.1016/j.sleep.2005.03.003