

Emerging Role of Electroencephalographic Aperiodic Activity in Anesthesia: A Narrative Review

Nathalie Demanet¹, M.D.,
Céline Khalifa, M.D., Ph.D.,
Mona Momeni, M.D., Ph.D.,
André Mouraux, M.D., Ph.D.,
Cédric Lenoir, Ph.D.



ANESTHESIOLOGY 2025; XXX:XX–XX

Since the development and use of electroencephalography (EEG) monitoring during general anesthesia, the interest of anesthesiologists in neurophysiology has considerably increased.¹ Indeed, various indices obtained from processed EEG monitors may represent accessible and noninvasive biomarkers to monitor brain activity and evaluate the depth of anesthesia. Intraoperatively, EEG oscillation power is computed and displayed on the screen of processed EEG monitors, and the patient's brain activity is based on well known canonical frequency bands (slow [0.1 to 1 Hz], delta [1 to 4 Hz], theta [4 to 8 Hz], alpha [8 to 12 Hz], beta [12 to 5 Hz], and gamma [25 to 80 Hz]) that compose the EEG spectrum.² The effects of anesthesia on these EEG frequency bands create characteristic patterns that can be used to infer the level of anesthesia, depending on the mechanisms of action of each drug.² Importantly, it has been shown that the power spectrum of human EEG,

ABSTRACT

Perioperative electroencephalography (EEG) has been widely studied in the last decade, not only as a useful brain state monitor but also as a potential tool to identify vulnerable patients at risk of perioperative neurocognitive disorders. Current literature has mostly focused on the oscillatory components of the EEG signal. Recently, interest in the functional role of the aperiodic activity of the EEG signal has increased both in neuroscience and in anesthesiology. This narrative review aims to provide clinicians and researchers with practical and methodologic insights into characterizing aperiodic EEG activity, focusing on its neurophysiological significance in neuroscience and anesthesia. It furthermore provides the reader with observed variations of aperiodic activity and periodic activity during general anesthesia and highlights whether those parameters could be useful to infer cognitive frailty and perioperative neurocognitive disorders and monitor depth of anesthesia during surgery.

(ANESTHESIOLOGY 2025; XXX:XX–XX)

and thus its canonical frequency bands, are composed of both periodic (spectral peaks) and aperiodic components. The aperiodic component is reflected in the spectrum as an exponential decay of power across frequencies, with an increased power of the aperiodic activity as the frequencies decrease.³ Recently, the physiologic significance of this aperiodic activity has gained interest in clinical and fundamental research.⁴ Traditionally considered as “noise,” aperiodic brain activity has been recently suggested to play a role in transitions between different brain states.⁵ This finding is particularly relevant for anesthesia, since variations of the EEG aperiodic activity might bring additional insights into cortical dynamics under different anesthetic states.

Understanding Aperiodic Activity

Aperiodic activity can be observed once the time domain EEG signal has been transformed into the frequency domain using, for instance, a Fourier transform.⁶ On the resultant power spectrum, nonoscillatory activity manifests as a decrease in power as a function of frequency, subscribing to a power law of $S(f) \propto 1/f^b$ (where S indicates power,

Submitted for publication April 22, 2025. Accepted for publication August 06, 2025.

Nathalie Demanet, M.D.: Department of Anesthesiology, Cliniques Universitaires Saint-Luc, Brussels, Belgium.

Céline Khalifa, M.D., Ph.D.: Department of Anesthesiology, Cliniques Universitaires Saint-Luc, Brussels, Belgium; Institute of Experimental and Clinical Research, UCLouvain, Brussels, Belgium; Institute of Neuroscience, UCLouvain, Brussels, Belgium.

Mona Momeni, M.D., Ph.D.: Department of Anesthesiology, Cliniques Universitaires Saint-Luc, Brussels, Belgium; Institute of Experimental and Clinical Research, UCLouvain, Brussels, Belgium; Institute of Neuroscience, UCLouvain, Brussels, Belgium.

André Mouraux, M.D., Ph.D.: Institute of Neuroscience, UCLouvain, Brussels, Belgium.

Cédric Lenoir, Ph.D.: Institute of Neuroscience, UCLouvain, Brussels, Belgium.

Copyright © 2025 American Society of Anesthesiologists. All Rights Reserved. ANESTHESIOLOGY 2025; XXX:XX–XX. DOI: 10.1097/ALN.0000000000005724

Abbreviations: EEG, electroencephalography; E/I, excitation/inhibition; EMG, electromyography; F000F, fitting oscillations and one-over-F; GABA, γ -aminobutyric acid; IRASA, irregular resampling auto-spectral analysis; LFP, local field potential; LOC, loss of consciousness

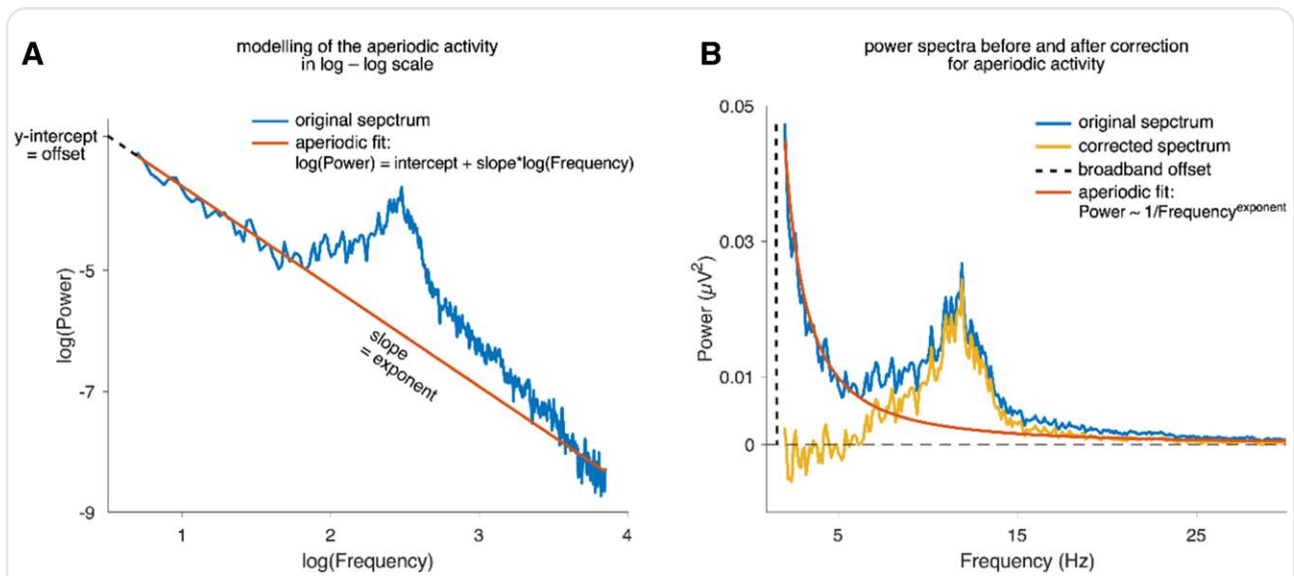


Fig. 1. Illustration of periodic and aperiodic activity on the electroencephalography (EEG) power spectrum (blue curve) of a single patient under general anesthesia before and after extraction of the $1/f$ activity. (A) Aperiodic activity represented in log-log scale, the aperiodic activity follows a linear decay (red line) characterized by the offset (y intercept) and the exponent (slope). (B) Corrected spectrum (yellow curve) illustrating the EEG power spectrum after subtraction of the aperiodic fit (red curve), with broadband offset (dashed black line) representing the difference in power between the magnitudes of the lowest and highest frequencies.

f indicates frequency, and β indicates exponent; fig. 1B),⁷ with lower frequencies exhibiting the greater amplitudes and higher frequencies exhibiting the lower amplitudes. This $1/f$ -like power law has been proposed to reflect the aperiodic activity³ and is thought to represent the underlying background arrhythmic activity of the brain.³ Oscillatory activity is reflected in the resulting magnitude, or power spectrum, by peaks or bumps superimposed on the decay representing aperiodic activity (fig. 1B).

While it is well known that periodic oscillations represent synchronized activity of neuronal populations, the precise neurobiological mechanisms underlying aperiodic activity remain under extensive investigation and debate.⁸ Two quantitative parameters are used to characterize the aperiodic activity: the aperiodic exponent (or slope) and the broadband offset. The offset in the log-log space representation is defined by the y -intercept of the power spectrum (fig. 1A).

The $1/f$ exponent (β), or spectral slope, quantifies the rate of power decrease with increasing frequency along the EEG spectrum. The exponent is usually measured using methods such as linear regression on log-log transformed power spectra⁹ (fig. 1A). It is suspected to reflect the balance between excitatory and inhibitory neurotransmissions in cortical circuits.²⁻⁴ Changes in the exponent have been linked to different physiologic and cognitive states, including anesthesia.⁸ More specifically, the steepness of this negative slope represents a marker of neural activity balance. For instance, steeper slopes (higher exponent values) have been associated with higher inhibitory processes. This is

consistent with slope changes observed during the use of γ -aminobutyric acid A (GABA_A) agonists, such as propofol.^{8,10} On the contrary, flatter or less negative slopes (lower exponent value) have been linked to excitatory or facilitatory neuronal states. Such slope changes could be observed during the use of ketamine, which induces a disinhibition of excitatory glutamatergic neurons and a dissociative state by blocking the activity of cortical inhibitory interneurons.¹⁰ Beyond its relevance to anesthesia, the aperiodic slope brings also other clinical insights into various brain states and disorders. For example, deeper stages of sleep, such as slow-wave sleep, are associated with steeper aperiodic slopes, while wakefulness and rapid eye movement sleep are associated with flatter slopes.^{11,12} A flatter slope could also reflect poor neural regulation due to specific treatments in patients suffering from schizophrenia¹³ or constitute a potential marker of seizure susceptibility in epileptic patients.¹⁴

The broadband offset of the EEG power spectrum represents the overall shift in power across all frequencies or the difference in power between the magnitude of the lowest and highest frequencies of the considered range (fig. 1B). The offset is more directly related to the total amount of neural activity. A higher offset value indicates a greater overall neural activity, while a lower offset value would indicate a general suppression of brain activity.^{3,9} However, as illustrated by Donoghue *et al.*,³ careful parameterization, particularly of the frequency range, is essential to avoid misinterpreting variations in broadband offset power and therefore mischaracterizing changes in oscillatory activity. An increase in the aperiodic exponent can lead to a reduction

in broadband offset power, which may be erroneously interpreted as a global decrease in neuronal activity when analyses are restricted to a narrow frequency band of interest.³

Similarly to the $1/f$ exponent, the broadband offset could provide some information about cortical excitability and brain function, which is particularly relevant for monitoring the depth of anesthesia. Indeed, an increase in broadband offset might indicate a gradual loss of consciousness using GABA-mediated hypnotics,^{15,16} while a decrease of the offset value could be a potential marker of emergence from anesthesia.¹⁷

Methodologic Approaches

Two toolboxes with different approaches are frequently used to characterize the aperiodic EEG activity, the fitting oscillations and one-over- f (FOOOF),³ and the irregular resampling auto-spectral analysis (IRASA).¹⁸ The IRASA algorithm estimates the aperiodic component by up- and down-resampling the time domain signal using several resampling factors and their inverse. Then, each pair of resampled power spectra is averaged, and the median of all averaged spectra is used to isolate the aperiodic slope in log-log space.¹⁸

Alternatively, the FOOOF algorithm estimates a linear fit of the EEG power spectra in log-log space and then removes it to flatten the spectrum. Subsequently, oscillatory components are fitted iteratively using a Gaussian model from the flattened spectrum and subtracted from the original spectrum to isolate the aperiodic component.¹⁹ From both methods, a linear fit of the power spectra gives an estimate of the y-intercept (offset) and slope (exponent).

The advantages and disadvantages of both algorithms have been thoroughly examined by Gerster *et al.*⁹ with the objective of offering recommendations and avoiding parameterization errors. The primary distinction between these two methods lies in their approach to parameterization. FOOOF is well suited for studies that require explicit parameterization of oscillatory and aperiodic components, with case-by-case definition of the fitting ranges. As the selection and parameterization of the toolbox may influence the results, the choice of the fitting range depends on the goal of the study and the properties of the data. For instance, when comparing the $1/f$ exponent across conditions, the presence of stronger low-frequency (e.g., delta) oscillations in one condition may elevate the y-intercept if the fitting range begins at 1 Hz, potentially resulting in a steeper $1/f$ slope.⁹ In contrast, IRASA is more appropriate for applications that prioritize a clear separation of periodic and aperiodic activity without the need for explicit parameterization, typically employing a broadband fitting range.⁹

In addition to these two methods, detrended fluctuation analysis offers an alternative way to characterize the EEG activity by focusing on the temporal dynamics of signal fluctuations.^{20,21} The output of this analysis (Hurst exponent) is conceptually and mathematically related to the aperiodic

exponent obtained from ISARA or FOOOF approaches and offers complementary insights for EEG analysis.

Finally, changes in $1/f$ slopes should be compared and controlled under conditions in which electromyography (EMG) activity, or any other activity affecting the EEG spectrum, is comparable to allow for a valid interpretation of $1/f$ slope variations. Donoghue *et al.*³ reported that significant correlations can be observed between the scalp distribution of the aperiodic exponent and the scalp distribution of certain frequency bands. The assessment of those different scalp topographies and the selection of channels of interest are likely important considerations to ensure fair interpretations of changes in periodic and aperiodic activities.²²

Neurophysiologic Implications

Cognitive Neuroscience

Aperiodic activity has been extensively studied in the previous decade. In 2017, Gao *et al.* developed a computational model, based on published and validated data from rats and macaques, to demonstrate the relationship between changes in the neural excitation/inhibition (E/I) balance and the exponent (β) of the $1/f$ decay.²³ They simulated local field potential (LFP), which represents a linear summation of total excitatory and inhibitory currents recorded from populations of cells in the vicinity of the electrode and reflecting collective neural dynamics.²⁴ By increasing inhibitory inputs received by the network simulating LFP activity and then reducing the E/I ratio, they found a steeper $1/f$ slope from the aperiodic activity. This result was then validated *in vivo* by administering propofol to macaque monkeys leading to steeper power spectra.²³ The $1/f$ slope, as a reflection of the excitation/inhibition balance within recurrent neural networks, is related to cognitive changes that parallel aging.^{25,26} Greater asynchronous neural activity and decline in cognitive performance are related to decreased exponent and intercept, resulting in a flatter $1/f$ slope.^{7,26} In 2023, Dziego *et al.*⁷ studied fluctuations in oscillatory and aperiodic activity alongside three standard computerized cognitive tasks. Their objective was to assess visual statistical learning ability, working memory capacity, and spatial imagery proficiency throughout a dynamic and complex cognitive task integrating dynamically changing information over time. They observed that a higher intercept has been related to a potential better neural network communication allowing enhanced performance.⁷ A higher intercept potentially reflecting an increased neural population spiking.^{27,28} These results support previous study by Immink *et al.*²⁹ demonstrating a positive correlation between higher intercept and enhanced visuomotor learning. To demonstrate a relationship between information processing and aperiodic $1/f$ activity, Gyurkovics *et al.*³⁰ analyzed broadband changes in EEG during an auditory task both before and after removing event-related potentials as confounding factors. They found significant modification in $1/f$ activity

in lower frequencies (between 2 and 25 Hz) explained by an increased inhibition following stimulus onset. Furthermore, the breadth of the $1/f$ modification between postevent and pre-event was related to the attentional demands of the task.

Aperiodic activity also varies with level of arousal, human sleep cycle, exogenous stimuli, and cognitive demands.¹⁹ A steeper slope has been observed in non-rapid eye movement sleep reflecting a state of increased inhibition.^{11,31} These results reflect the complexity of the physiologic mechanisms underlying this EEG component whose functional role remains controversial.

Neuropathology

Aperiodic activity is variable and dynamic within and between subjects according to clinical diagnoses. Subjects with attention deficit hyperactivity disorder,^{32,33} schizophrenia,^{13,34} and autism spectrum disorders³⁵ showed altered $1/f$ slopes when compared to neurotypical controls. A flatter slope was observed in both attention deficit hyperactivity disorder and autism spectrum disorders, whereas patients with schizophrenia exhibited a steeper slope. Alteration in the aperiodic component was also investigated in relation to symptom severity in Parkinson's disease.³⁶

EEG, typically regarding to its power modification across canonical frequency bands, may also be used as a tool to help treating and predicting outcomes for patients suffering from stroke.³⁷ In 2022, Lanza *et al.*³⁸ demonstrated a decreased E/I ratio, leading to a steeper $1/f$ slope and a lower exponent (β), occurring after an ischemic stroke. Exponent normalization correlated with clinical improvement. A few studies suggest that aperiodic activity could be superior to oscillatory activity in assessing patients' level of consciousness and outcomes following traumatic brain injury and stroke, making the exponent (β) a potential future marker to monitor states of reduced consciousness such as minimally conscious state, status epilepticus and coma.^{5,11}

Clinical Application in Anesthesiology

Excitation/Inhibition Ratio

Colombo *et al.*¹⁰ demonstrated that in healthy subjects, loss of consciousness induced by xenon and propofol administration led to an increase of the exponent (β), *i.e.*, a steeper $1/f$ slope. This pattern was potentially due to the changes in neural E/I ratio with an increase in inhibition mediated by propofol GABA_A potentiation. Potentiation of GABA_A receptors results in reduced action potential generation and enhanced hyperpolarization within the thalamocortical system, leading to a steeper $1/f$ slope.³⁹ The mode of action of xenon on E/I ratio remains unclear. Although acting as a noncompetitive inhibitor of *N*-methyl-D-aspartate receptor, xenon generates neuronal disfacilitation, a type of inhibition characterized by neuronal hyperpolarization resulting from a temporary lack of excitatory synaptic input,⁴⁰ similar to active inhibition.¹⁰ Ketamine administration induced

slight reduction in the exponent (β). Nonetheless, an overlap was observed between the exponent (β) obtained during ketamine administration and during wakefulness across participants.¹⁰ Interestingly a recent study suggested that aperiodic activity is driven by the E/I ratio but was not a reliable measure of this ratio due to the physiologic properties of GABA and α -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor membrane potentials.⁸

Several studies have reported propofol-induced changes in the slope in the 30- to 45-Hz range, spectral slope in high frequency emerging as a reliable marker of arousal level variations under anesthesia.^{5,10,11,23,41} Brake *et al.*⁸ studied the influence of a fixed rate propofol infusion on the aperiodic activity in 14 patients. They analyzed the EEG with the FOOOF algorithm and observed an increase in the exponent (β) before loss of consciousness, followed by a plateau phase, corresponding to a steepening in the power spectrum around the 25-Hz frequency range.⁸

Current Literature in the Field of Anesthesiology

Exponent as a Potential Marker of Unconsciousness and Emergence

In a recent study, Zhang *et al.*⁴¹ investigated the potential of aperiodic activity as a marker of anesthetic depth. Changes in the $1/f$ slope were analyzed during an ultra-slow propofol infusion protocol in healthy participants. Transitions between different states of consciousness, including the presence of reactivity, loss of behavioral responsiveness, loss of consciousness (LOC), and recovery of reactivity, were identified based on response latency to auditory stimuli. Their findings indicated that the $1/f$ slope was significantly correlated with the state of consciousness. Compared to wakefulness, the $1/f$ slope steepened (*i.e.*, the exponent [β] increased) during loss of behavioral responsiveness and continued to steepen during loss of consciousness. A steeper spectral slope was also associated with the transition from light to deep sedation. During recovery, the spectral slope became progressively flatter (*i.e.*, decrease of the exponent [β]).⁴¹

In a prospective study, Leroy *et al.*¹⁵ characterized both the offset and exponent (β) during the transition to propofol-induced unconsciousness in a cohort of young (18 to 30 yr old) and elderly (70 yr or older) patients. Consistent with findings of Zhang *et al.*,⁴¹ the results of Leroy *et al.*¹⁵ showed an increase in the exponent (β), *i.e.* a steeper slope, in both groups at time of loss of consciousness corresponding to an increased inhibition. The elderly cohort reported an earlier increase of the exponent (β) occurring between the pre-LOC time window (defined as 105 to 75s before LOC) and LOC. They also reported a decrease of the exponent shortly before LOC in both groups, more pronounced in the young group, possibly reflecting a phenomenon of paradoxical excitation.⁴² Regarding the offset, they observed an increase between pre-LOC and LOC in both groups. The young group showed a further increase of the offset in the post-LOC time window defined between 190 and

Table 1. Included Anesthesiology Studies on Aperiodic Features

Study, Year	Study Design	Study Population	Anesthetic Protocol	EEG Features	Aperiodic Activity's Toolboxes	Phase of Anesthesia	Studied Aperiodic Components	Outcome/Endpoint
Kaiser <i>et al.</i> (2020) ⁴³	Prospective observational study	589 patients undergoing cardiac surgery with CPB	Propofol induction, maintained with isoflurane	Scalp EEG using Narcotrend (Narcotrend Group, Germany) DoA monitor	Aperiodic broadband measured as the y -intercept value of a linear regression on PSD; no toolbox mentioned	Maintenance, pre-CPB	Broadband offset across frequencies of 0.5–4 and 7–17 Hz	Broadband power is correlated with comorbidities, MAC and age; association between comorbidities, MAC, age, and peak alpha power is markedly reduced when the underlying broadband effect is subtracted
Kreuzer <i>et al.</i> (2020) ⁴⁴	Retrospective	Clinical EEG data sets from 180 patients; two cohorts: youngest quartile group (18 to 43 yr old) and oldest quartile group (73 to 90 yr old)	Propofol induction, maintained with sevoflurane	Frontal EEG: Bispectral Index (Medtronic, Ireland) or Entropy Module (GE Healthcare, Finland) monitors	F000F algorithm	Maintenance; before the onset of surgery	Exponent and broadband offset	Oldest quartile exhibited a significant decrease in both the exponent and the offset
Leroy <i>et al.</i> (2023) ¹⁵	Prospective	23 patients: 2 cohorts: young (18–30 yr old) and elderly (≥70 yr old)	Propofol induction	10- to 20-system scalp EEG	F000F algorithm	LOC	Exponent, offset	Increase in exponent and offset in both cohorts
Widmann <i>et al.</i> (2025) ³⁹	Retrospective	Clinical EEG data sets	Maintenance with propofol, sevoflurane or desflurane	10- to 20-system scalp EEG	F000F algorithm	LOC and midsurgery maintenance	Exponent α (using inverse power law $PSD(f) = 1/f^\beta$)	Exponent increased from consciousness to unconsciousness

CPB, cardiopulmonary bypass; DoA monitor, depth-of-anesthesia monitor; EEG, electroencephalography; F000F, fitting oscillations and one-over-F; LOC, loss of consciousness; MAC, minimal alveolar concentration; PSD, power spectral density.

220s after LOC.¹⁵ Steepening of the slope during loss of consciousness was confirmed by several recent studies,^{39,41} in which an increase of the exponent was observed after loss of consciousness, allowing consideration of the exponent (β) as a potential biomarker to improve discrimination between consciousness and unconsciousness. On the contrary, emergence was marked by a decrease of the exponent (β), suggesting that it could be used as a potential electroencephalographic marker of arousal.^{11,17,31,41} The summary characteristics of the above-mentioned clinical research studies on aperiodic features, involving patients undergoing surgery, are detailed in table 1.

Age-related Feature of the Aperiodic Activity and Depth-of-anesthesia Monitoring. As mentioned previously, a decreased exponent, resulting in a flatter 1/f slope, is observed in elderly populations.^{26,45} This observation has been assumed to be the consequence of greater asynchronous neural activity and seems to parallel the cognitive decline observed in this population.^{7,26} Under general anesthesia, elderly patients exhibit a reduction of the spectral magnitude of the EEG signal mainly in the alpha frequency range.⁴⁶ To assess whether variations of the broadband offset is in part responsible for this power reduction, a few studies subtracted the underlying aperiodic activity from the power spectral density signal. Leroy *et al.*¹⁵ observed similar spectrogram in the alpha, beta, and low gamma frequency bands in elderly and young patients after removing the aperiodic fit. This suggested a significant impact of the aperiodic component on age-related power modifications. This was in line with the results of Kaiser *et al.*⁴³ showing a major reduction in oscillatory alpha power correlated with age, comorbidities and minimal alveolar concentration once aperiodic activity had been subtracted. In 2020, Kreuzer *et al.*⁴⁴ demonstrated that aging alters the aperiodic components of the EEG in patients under general anesthesia by comparing EEG recordings from the youngest and oldest quartiles of the study population. Older patients exhibited a flatter 1/f slope compared to younger patients. In addition, the offset was significantly decreased in the elderly group. The described relationship between aperiodic component and age may provide new considerations for further development of processed EEG monitors, especially in cognitively frail patients with comorbidities.

Regarding available depth of anesthesia, although depth-of-anesthesia monitors like Bispectral Index (Medtronic, USA) are often described as relying on oscillatory power ratios (*e.g.*, 30 to 47 Hz *vs.* 11 to 20 Hz).⁴⁷ It has been recently suggested that they predominantly track broadband attenuations in high-frequency EEG power.³⁹ This operational mechanism closely parallels the aperiodic exponent (β) approach, meaning that both methods quantify essentially the same neurophysiological change: the steepening of the EEG's 1/f slope with sedation, either implicitly (in processed EEG indices) or explicitly (through β -exponent analysis). Similar mechanisms may be assumed

for other depth-of-anesthesia monitors, such as SedLine (Masimo Corporation, USA) or Narcotrend (Narcotrend Group, Germany). Notably, Schuller *et al.*⁴⁸ recently investigated the influence of electromyographic activity on the indices generated by depth-of-anesthesia monitoring devices. They demonstrated that the GE Entropy monitor (GE HealthCare, Finland) produces values consistent with deep sedation or anesthesia in awake subjects undergoing neuromuscular block, due to its reliance on EMG activity. When EEGs recorded during drug-induced paralysis on 11 volunteers were submitted to the entropy monitor, both state entropy (a measure of the irregularity of the EEG signal in the 0.8- to 32-Hz range) and response entropy (an extended entropy index calculated greater than 0.8- to 47-Hz, including both EEG and high-frequency EMG components) significantly decreased despite preserved consciousness. A marked reduction in EEG power spectrum was observed, suggesting a steepening of the 1/f slope, most prominently above 20 Hz but also within the delta and theta bands.⁴⁸ These results indicated the importance of accounting for muscle activity in depth-of-anesthesia monitors such as the entropy monitoring to ensure accurate interpretation of variations of the frequency content of the EEG during both wakefulness and anesthesia.

A Biomarker for Postoperative Delirium? More and more studies on aperiodic activity have been carried out in the anesthesiology field to determine its clinical relevance as a potential biomarker of cognitive frailty. In a recent study, Lendner *et al.*⁴⁹ investigated the impact of general anesthesia on brain activity associated with memory function in patients aged 60 and older undergoing prostatectomy. Specifically, they examined oscillatory and aperiodic EEG dynamics 1 day before and 2 to 3 days after surgery, using both neuropsychological assessment and a visual working memory task. They observed a general decline in verbal learning following anesthesia compared to preoperative performance. Notably, patients who exhibited a flatter 1/f spectral slope after anesthesia demonstrated better performance on verbal memory tasks, in terms of both word recall and learning rate. This study suggested that aperiodic activity may serve as an electrophysiologic biomarker for evaluating postoperative cognitive function.⁴⁹ Regarding postoperative delirium, Ostertag *et al.*¹⁷ investigated the difference in aperiodic broadband offset and exponent between patients with and without postanesthesia care unit delirium. EEG was recorded during emergence. No difference was observed on the exponent. However, offset was significantly higher in patients without delirium. More important, the aperiodic components did not improve discrimination between patients with and without delirium compared with conventional frontal α -band power analysis.¹⁷ One observational study¹⁶ aimed to identify EEG predictors of postoperative delirium by recording and analyzing the EEG of patients the day before surgery and 1, 2, and 15 min after propofol-induced loss of consciousness. Patients who developed postoperative

delirium showed a decreased power in the alpha and beta bands at 1 min after loss of consciousness and a decreased broadband offset at 15 min after LOC as compared to before surgery. In brief, in these studies, postoperative delirium was associated with a decreased aperiodic offset suggesting lower overall neural activity and greater cognitive frailty. Future research will need to determine the potential utility of aperiodic activity in assessing cognitive impairment and preventing postoperative delirium.

Conclusions and Perspectives

Aperiodic activity, previously dismissed as noise in traditional EEG analyses, has emerged as a potential significant component in understanding neural dynamics. The aperiodic activity offset and 1/f slope, influenced by the excitation/inhibition (E/I) balance, have been linked to cognitive performance, aging, and various neuropathological conditions. Their modifications during propofol-induced loss of consciousness and emergence and according to age and cognitive function can potentially be used to identify cognitive frailty and to perform an optimized EEG-based anesthesia. Despite these promising insights, current literature has not established a superiority of aperiodic activity over oscillatory activity as a biomarker of cognitive frailty. However, several studies suggest a major role of aperiodic activity in age-related spectral modifications under general anesthesia, potentially influencing the output of currently available depth-of-anesthesia monitors as the reflection of a combination of both oscillatory and aperiodic activity. Moreover, aperiodic activity could be used as a potential electroencephalographic marker to improve discrimination between consciousness and unconsciousness. Future research is required to examine its clinical applications and suitability for implementation in processed EEG monitors.

Research Support

Support was provided solely from institutional and/or departmental sources.

Competing Interests

The authors declare no competing interests.

Correspondence

Address correspondence to Dr. Demanet: Cliniques Universitaires Saint-Luc, Avenue Hippocrate, 10, 1200 Brussels, Belgium. nathalie.demanet@saintluc.uclouvain.be

References

1. Marchant N, Sanders R, Sleight J, et al.: How electroencephalography serves the anesthesiologist. *Clin EEG Neurosci* 2014; 45:22–32. doi:10.1177/1550059413509801

2. Purdon PL, Sampson A, Pavone KJ, Brown EN: Clinical electroencephalography for anesthesiologists: Part I: Background and basic signatures. *ANESTHESIOLOGY* 2015; 123:937–60. doi:10.1097/ALN.0000000000000841
3. Donoghue T, Haller M, Peterson EJ, et al.: Parameterizing neural power spectra into periodic and aperiodic components. *Nat Neurosci* 2020; 23:1655–65. doi:10.1038/s41593-020-00744-x
4. Pani SM, Saba L, Fraschini M: Clinical applications of EEG power spectra aperiodic component analysis: A mini-review. *Clin Neurophysiol* 2022; 143:1–13. doi:10.1016/j.clinph.2022.08.010
5. Maschke C, Duclos C, Owen AM, Jerbi K, Blain-Moraes S: Aperiodic brain activity and response to anesthesia vary in disorders of consciousness. *Neuroimage* 2023; 275:120154. doi:10.1016/j.neuroimage.2023.120154
6. Welch P: The use of fast Fourier transform for the estimation of power spectra: A method based on time averaging over short, modified periodograms. *IEEE Trans Audio Electroacoust* 1967; 15:70–3. doi:10.1109/tau.1967.1161901
7. Dziego CA, Bornkessel-Schlesewsky I, Jano S, et al.: Neural and cognitive correlates of performance in dynamic multi-modal settings. *Neuropsychologia* 2023; 180:108483. doi:10.1016/j.neuropsychologia.2023.108483
8. Brake N, Duc F, Rokos A, et al.: A neurophysiological basis for aperiodic EEG and the background spectral trend. *Nat Commun* 2024; 15:1514. doi:10.1038/s41467-024-45922-8
9. Gerster M, Waterstraat G, Litvak V, et al.: Separating neural oscillations from Aperiodic 1/f activity: Challenges and recommendations. *Neuroinformatics* 2022; 20:991–1012. doi:10.1007/s12021-022-09581-8
10. Colombo MA, Napolitani M, Boly M, et al.: The spectral exponent of the resting EEG indexes the presence of consciousness during unresponsiveness induced by propofol, xenon, and ketamine. *Neuroimage* 2019; 189:631–44. doi:10.1016/j.neuroimage.2019.01.024
11. Lendner JD, Helfrich RF, Mander BA, et al.: An electrophysiological marker of arousal level in humans. *eLife* 2020; 9:e55092. doi:10.7554/eLife.55092
12. Pani SM, Fraschini M, Figorilli M, Tamburrino L, Ferri R, Puligheddu M: Sleep-related hypermotor epilepsy and non-rapid eye movement parasomnias: Differences in the periodic and aperiodic component of the electroencephalographic power spectra. *J Sleep Res* 2021; 30:e13339. doi:10.1111/jsr.13339
13. Molina JL, Voytek B, Thomas ML, et al.: Memantine effects on electroencephalographic measures of putative excitatory/inhibitory balance in schizophrenia. *Biol Psychiatry Cogn Neurosci Neuroimaging* 2020; 5:562–8. doi:10.1016/j.bpsc.2020.02.004
14. Roche KJ, LeBlanc JJ, Levin AR, O’Leary HM, Baczewski LM, Nelson CA: Electroencephalographic spectral power as a marker of cortical function and disease severity in girls with Rett syndrome. *J Neurodev Disord* 2019; 11:15. doi:10.1186/s11689-019-9275-z
15. Leroy S, Major S, Bubltz V, Dreier JP, Koch S: Unveiling age-independent spectral markers of propofol-induced loss of consciousness by decomposing the electroencephalographic spectrum into its periodic and aperiodic components. *Front Aging Neurosci* 2023; 14:1076393. doi:10.3389/fnagi.2022.1076393
16. Pollak M, Leroy S, Röhr V, Brown EN, Spies C, Koch S: Electroencephalogram biomarkers from anesthesia induction to identify vulnerable patients at risk for postoperative delirium. *ANESTHESIOLOGY* 2024; 140:979–89. doi:10.1097/ALN.0000000000004929
17. Ostertag J, Engelhard A, Nuttall R, et al.: Development of postanesthesia care unit delirium is associated with differences in aperiodic and periodic alpha parameters of the electroencephalogram during emergence from general anesthesia: Results from a prospective observational cohort study. *ANESTHESIOLOGY* 2024; 140:73–84. doi:10.1097/ALN.0000000000004797
18. Wen H, Liu Z: Separating fractal and oscillatory components in the power spectrum of neurophysiological signal. *Brain Topogr* 2016; 29:13–26. doi:10.1007/s10548-015-0448-0
19. Donoghue T, Schaworonkow N, Voytek B: Methodological considerations for studying neural oscillations. *Eur J Neurosci* 2022; 55:3502–27. doi:10.1111/ejn.15361
20. Díaz M. HA, Córdova F: On the meaning of Hurst entropy applied to EEG data series. *Procedia Comput Sci* 2022; 199:1385–92. doi:10.1016/j.procs.2022.01.175
21. Hardstone R, Poil S-S, Schiavone G, et al.: Detrended fluctuation analysis: A scale-free view on neuronal oscillations. *Front Physiol* 2012; 3:450. doi:10.3389/fphys.2012.00450
22. Gasser T, Schuller JC, Gasser US: Correction of muscle artefacts in the EEG power spectrum. *Clin Neurophysiol* 2005; 116:2044–50. doi:10.1016/j.clinph.2005.06.002
23. Gao R, Peterson EJ, Voytek B: Inferring synaptic excitation/inhibition balance from field potentials. *Neuroimage* 2017; 158:70–8. doi:10.1016/j.neuroimage.2017.06.078
24. Katzner S, Nauhaus I, Benucci A, Bonin V, Ringach DL, Carandini M: Local origin of field potentials in visual cortex. *Neuron* 2009; 61:35–41. doi:10.1016/j.neuron.2008.11.016
25. Hill AT, Clark GM, Bigelow FJ, Lum JAG, Enticott PG: Periodic and aperiodic neural activity displays age-dependent changes across early-to-middle childhood. *Dev Cogn Neurosci* 2022; 54:101076. doi:10.1016/j.dcn.2022.101076
26. Voytek B, Kramer MA, Case J, et al.: Age-related changes in 1/f neural

- electrophysiological noise. *J Neurosci* 2015; 35:13257–65. doi:10.1523/JNEUROSCI.2332-14.2015
27. Manning JR, Jacobs J, Fried I, Kahana MJ: Broadband shifts in local field potential power spectra are correlated with single-neuron spiking in humans. *J Neurosci* 2009; 29:13613–20. doi:10.1523/JNEUROSCI.2041-09.2009
 28. Miller KJ, Hermes D, Honey CJ, et al.: Human motor cortical activity is selectively phase-entrained on underlying rhythms. *PLoS Comput Biol* 2012; 8:e1002655. doi:10.1371/journal.pcbi.1002655
 29. Immink MA, Cross ZR, Chatburn A, Baumeister J, Schlesewsky M, Bornkessel-Schlesewsky I: Resting-state aperiodic neural dynamics predict individual differences in visuomotor performance and learning. *Hum Mov Sci* 2021; 78:102829. doi:10.1016/j.humov.2021.102829
 30. Gyurkovics M, Clements GM, Low KA, Fabiani M, Gratton G: Stimulus-induced changes in 1/f-like background activity in EEG. *J Neurosci* 2022; 42:7144–51. doi:10.1523/JNEUROSCI.0414-22.2022
 31. Miskovic V, MacDonald KJ, Rhodes LJ, Cote KA: Changes in EEG multiscale entropy and power-law frequency scaling during the human sleep cycle. *Hum Brain Mapp* 2019; 40:538–51. doi:10.1002/hbm.24393
 32. Ostlund BD, Alperin BR, Drew T, Karalunas SL: Behavioral and cognitive correlates of the aperiodic (1/f-like) exponent of the EEG power spectrum in adolescents with and without ADHD. *Dev Cogn Neurosci* 2021; 48:100931. doi:10.1016/j.dcn.2021.100931
 33. Arnett AB, Rutter TM, Stein MA: Neural markers of methylphenidate response in children with attention deficit hyperactivity disorder. *Front Behav Neurosci* 2022; 16:887622. doi:10.3389/fnbeh.2022.887622
 34. Peterson EJ, Rosen BQ, Belger A, Voytek B, Campbell AM: Aperiodic neural activity is a better predictor of schizophrenia than neural oscillations. *Clin EEG Neurosci* 2023; 54:434–45. doi:10.1177/15500594231165589
 35. Manyukhina VO, Prokofyev AO, Galuta IA, et al.: Globally elevated excitation–inhibition ratio in children with autism spectrum disorder and below-average intelligence. *Mol Autism* 2022; 13:20. doi:10.1186/s13229-022-00498-2
 36. Bush A, Zou JF, Lipski WJ, Kokkinos V, Richardson RM: Aperiodic components of local field potentials reflect inherent differences between cortical and subcortical activity. *Cereb Cortex* 2024; 34:bhae186. doi:10.1093/cercor/bhae186
 37. Finnigan S, Wong A, Read S: Defining abnormal slow EEG activity in acute ischaemic stroke: Delta/alpha ratio as an optimal QEEG index. *Clin Neurophysiol* 2016; 127:1452–9. doi:10.1016/j.clinph.2015.07.014
 38. Lanzone J, Colombo MA, Sarasso S, et al.: EEG spectral exponent as a synthetic index for the longitudinal assessment of stroke recovery. *Clin Neurophysiol* 2022; 137:92–101. doi:10.1016/j.clinph.2022.02.022
 39. Widmann S, Ostertag J, Zinn S, et al.: Aperiodic component of the electroencephalogram power spectrum reflects the hypnotic level of anaesthesia. *Br J Anaesth* 2025; 134:392–401. doi:10.1016/j.bja.2024.09.027
 40. Timofeev I, Grenier F, Steriade M: Disfacilitation and active inhibition in the neocortex during the natural sleep–wake cycle: An intracellular study. *Proc Natl Acad Sci USA* 2001; 98:1924–9. doi:10.1073/pnas.98.4.1924
 41. Zhang Y, Wang Y, Cheng H, et al.: EEG spectral slope: A reliable indicator for continuous evaluation of consciousness levels during propofol anesthesia. *Neuroimage* 2023; 283:120426. doi:10.1016/j.neuroimage.2023.120426
 42. Ibrahim AE, Taraday JK, Kharasch ED: Bispectral index monitoring during sedation with sevoflurane, midazolam, and propofol. *ANESTHESIOLOGY* 2001; 95:1151–9. doi:10.1097/00000542-200111000-00019
 43. Kaiser HA, Hirschi T, Sleigh C, et al.: Comorbidity-dependent changes in alpha and broadband electroencephalogram power during general anaesthesia for cardiac surgery. *Br J Anaesth* 2020; 125:456–65. doi:10.1016/j.bja.2020.06.054
 44. Kreuzer M, Stern MA, Hight D, et al.: Spectral and entropic features are altered by age in the electroencephalogram in patients under sevoflurane anesthesia. *ANESTHESIOLOGY* 2020; 132:1003–16. doi:10.1097/ALN.0000000000003182
 45. Leroy S, Bubltz V, von Dincklage F, Antonenko D, Fleischmann R: Normative characterization of age-related periodic and aperiodic activity in resting-state real-world clinical EEG recordings. *Front Aging Neurosci* 2025; 17:1540040. doi:10.3389/fnagi.2025.1540040
 46. Khalifa C, Lenoir C, Robert A, et al.: Intra-operative electroencephalogram frontal alpha-band spectral analysis and postoperative delirium in cardiac surgery: A prospective cohort study. *Eur J Anaesthesiol* 2023; 40:777–87. doi:10.1097/EJA.0000000000001895
 47. Connor CW: Open reimplementation of the BIS algorithms for depth of anesthesia. *Anesth Analg* 2022; 135:855–64. doi:10.1213/ANE.00000000000006119
 48. Schuller PJ, Pretorius JPG, Newbery KB: Response of the GE Entropy™ monitor to neuromuscular block in awake volunteers. *Br J Anaesth* 2023; 131:882–92. doi:10.1016/j.bja.2023.08.013
 49. Lendner JD, Harler U, Daume J, et al.: Oscillatory and aperiodic neuronal activity in working memory following anesthesia. *Clin Neurophysiol* 2023; 150:79–88. doi:10.1016/j.clinph.2023.03.005