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TECHNICAL REVIEW

Nonlinear dynamical analysis of sleep electroencephalography using fractal and entropy approaches

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SUMMARY

The analysis of electroencephalography (EEG) recordings has attracted increasing interest in recent decades and provides the pivotal scientific tool for researchers to quantitatively study brain activity during sleep, and has extended our knowledge of the fundamental mechanisms of sleep physiology. Conventional EEG analyses are mostly based on Fourier transform technique which assumes linearity and stationarity of the signal being analyzed. However, due to the complex and dynamical characteristics of EEG, nonlinear approaches are more appropriate for assessing the intrinsic dynamics of EEG and exploring the physiological mechanisms of brain activity during sleep. Therefore, this article introduces the most commonly used nonlinear methods based on the concepts of fractals and entropy, and we review the novel findings from their clinical applications. We propose that nonlinear measures may provide extensive insights into brain activities during sleep. Further studies are proposed to mitigate the limitations and to expand the applications of nonlinear EEG analysis for a more comprehensive understanding of sleep dynamics.

Background

Sleep, in contrast to wakefulness, is characterized by reduced awareness and responsiveness. A basic model of sleep homeostasis is based on the concept of sleep-wake transition [1]. Conventionally, sleep stages in humans are classified as wake, rapid eye movement (REM) sleep, and an approximate continuum of depth during non-REM (NREM) sleep based on electroencephalographic patterns, which comprises about 80% of the entire sleep [2]. This cycling model of wake/NREM/REM sleep switches has been the primary focus of sleep research for decades. However, this reductionist type of approach is over-simplified and has limitation in understanding pathophysiological mechanisms in sleep disorders.

Sleep is not simply a succession of human invented stages, but a delicate and sophisticated nonlinear symphony played by the brain in a democratic and mutual interaction with the rest of the body [2]. Real sleep stages are dynamic transitions between multiple physiological states swinging between the dual condition of stability and instability to warrant environmental adaptations and achieve physical and mental restoration [3].

Quantification of sleep stages via the analysis of electroencephalography (EEG) signal has been a challenge for years. Conventional visual sleep stage scoring is arbitrary and does not fully capture intrinsic EEG activity [4]. Fourier-based spectral analysis can quantify frequency compositions in EEG signals and is the most commonly used EEG analysis; however, it has intrinsic limitations to capturing underlying dynamics of the brain oscillations. First, fast Fourier transform (FFT)-based analysis assumes that complex oscillations embedded in the EEG signal are comprised of sine waves with different frequencies [5]. In this context, EEG signal can be decomposed into frequency components such as beta, alpha, theta, or delta frequency bands. However, it has long been known that brain oscillation is not a linear combination of these arbitrary frequency components, a property called "nonlinearity" [6]. Second, FFT-based spectral analysis assumes that none of these frequency components change in amplitude or shape as time evolves, which is clearly against what has been observed in complex brain oscillations, a property called "nonstationarity" [5].

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Abbreviations

ApEn	approximate entropy
AS	active sleep
CAP	cyclic alternating pattern
CD	correlation dimension
DFA	detrended fluctuation analysis
ECG	electrocardiography
EEG	electroencephalography
ESES	electrical status epilepticus during slow-wave sleep
FD	fractal dimension
FFT	fast Fourier transform
fMRI	functional magnetic resonance imaging
H	Hurst exponent
MSE	multiscale entropy
N1	nonrapid eye movement sleep stage 1
N2	nonrapid eye movement sleep stage 2
N3	nonrapid eye movement sleep stage 3
NREM	nonrapid eye movement
OSA	obstructive sleep apnea
PD	Parkinson disease
PSG	polysomnography
QS	quiet sleep
REM	rapid eye movement
SampEn	sample entropy
SWS	slow-wave sleep

It has long been observed that physiologic output of human body is nonstationary and nonlinear. Controls of physiological systems and outputs such as heartbeat, respiration, and brain wave oscillations are extraordinary complex [7]. Such complexity is believed to arise from nonlinear interactions among multiple control nodes in different physiological body systems that operate at multiple time scales. It has been hypothesized that the complexity of a biological system should be related to the system's capacity to adapt and function in an ever changing environment [7]. Conventionally, scientists employ a reductionist approach to disassemble the complex system into constituent pieces, examine each component, and, finally, reassemble them to recreate the original entity. However, this approach is often unrealistic. In most circumstances, we can observe only the macroscopic output of physiological functions, such as an EEG, heart rate, or respiration. In the language of complex systems, the composite behavior cannot be fully understood by "adding up" the components. Instead, one needs new approaches to measuring a system's integrative behavior. Thus, the understanding of the complex dynamics of the physiologic output, such as changes in EEG dynamics observed across different sleep stages, will be improved by applying nonlinear dynamical approaches to the analysis of EEG signal.

Nonlinear analysis of sleep EEG

The term *nonlinear* applies to systems in which components interact non-additively [8]. One example of the non-additivity is brain electrical activity that reflects combinations of excitatory and inhibitory postsynaptic potentials in apical dendrites of pyramidal neurons in the superficial layers of the cortex [9]. To understand the nonlinear feature of the EEG signal, in 1985, Rapp et al. pioneeringly performed a chaos analysis of spontaneous neural activity in monkeys [10], and Babloyantz et al. examined the correlation dimension (CD) of human sleep EEG [11]. At the early stages (1985–1990) and since 1990, nonlinear EEG analysis was mainly referred to low-dimensional chaotic dynamics and surrogate data testing, respectively [3]. In the late 1990s, phase synchronization and generalized synchronization became widely used. Recently, the concepts and methods originated from the chaos theory or complexity science has attracted considerable attention. Nonlinear approaches are suggested to be superior to traditional linear methods in understanding EEG dynamics [12]. In addition, the nonlinear approaches provide clearer insights into dynamical nature and variability of the brain signal and have shown their ability to surpass traditional spectral techniques, such as tracing epileptic changes in the EEG signal [13].

Quantification of the nonlinear features of sleep physiology is very important in two aspects: 1) for evaluating dynamical models of sleep homeostasis and 2) for clinically monitoring alteration/degradation of normal sleep physiology with aging and pathological conditions [8]. In the last two decades, novel approaches derived from concepts of nonlinear dynamics and statistical physics theories have been developed and applied to probe generic features of complex systems. These approaches revealed that the fluctuations in the outputs of these systems contain important information about the underlying mechanisms of system controls. For instance, robust fractal/scale-invariant, multifractal, and time irreversibility were observed in healthy physiologic systems (indicating complex physiological control) and the alterations of these nonlinear statistical properties are associated with aging and pathological states [8,14]. Moreover, certain generic features exist in a various number of physiological systems (e.g., similar scale-invariant correlations in heartbeat fluctuations, motor activity, gait, respiration, and brain wave oscillations), indicating a universal "rule" in the underlying mechanisms of nonlinear interactions in physiological systems. These universal features of different physiological systems provide an important guidance for building physiologically meaningful models of integrative physiological systems.

Nonlinear dynamics theory provides new opportunities for the understanding of sleep EEG behavior [15], and increasing amount of studies have used nonlinear methods to investigate the characteristics of brain activities during sleep. In this article, we therefore present the most commonly used nonlinear analyses of sleep EEG signal, such as fractal or entropy methods, and review their applications to sleep studies. This review intends to inspire future sleep studies to understand the complex nature of sleep physiology, particular the dynamical changes in brain activity during sleep.

Fractal-based methods

Mandelbrot [16] introduced the *fractal* theory, which can be expressed by two phenomenon: self-similarity and fractional dimensionality. Fractal theory has been used for explaining natural landscapes, modeling temporal dynamics of a time series, and predicting extreme events or human behavior [17]. Therefore, fractal analysis has potential to describing the dynamics of brain electrical activities under physiological and pathological conditions. To quantify fractal scaling behavior in a time series, several methods have been developed to quantify the fractal dimension, including the CD, Hurst exponent (H), and detrended fluctuation analysis (DFA).

Correlation dimension

The correlation dimension (CD, or D_2 in certain literature) [18] describes the fractional dimensionality of an underlying process in relation to its geometrical reconstruction in embedded phase

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