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Symbolic dynamics of electroencephalography is associated with the sleep depth and overall sleep quality in healthy adults

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HIGHLIGHTS

- Symbolic dynamics of EEG may assist the continuous measurement of sleep depth.
- Average P CW of EEGs may be used as an indicator for timely sleep quantification.
- Results support the use of nonlinear EEG analysis in automatic sleep evaluation.

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ABSTRACT

Sleep electroencephalographic (EEG) provides the opportunity to study sleep scientifically. Slow wave activity (SWA), presenting EEG spectral power in the low-frequency range, has proven to be a useful parameter in sleep medicine. Drawing inspiration from the adaptive and noise-assist features of symbolic dynamics, we introduced a symbolic analogue of SWA as EEG signal was generally considered as non-linear and non-stationary. Moreover, we investigated whether the proposed metrics can capture patterns that characterize and differentiate different sleep stages, and whether EEG dynamical features during the wake to sleep transition after light-off share a correlation with the overall sleep quality during the whole night. Single-channel EEGs derived from the polysomnography (PSG) of 111 healthy adults in the Sleep Heart Health Study were analyzed retrospectively. Every 30-second epoch of EEG data was transformed into a symbolic sequence using equiprobable symbolization and then the percentage of constant word (P_{CW}) was calculated. The results revealed that the proposed metric, P_{CW}, exhibits a correlation with wake/sleep stages over the night. More importantly, average P_{CW} in short sections (15–60 min) at the beginning of the night shows a correlation with various indices of sleep quality for the entire night, suggesting P_{CW} as a potential indicator for the requirement for an early sleep intervention. In conclusion, the results validate the use of symbolic dynamics in automatic sleep scoring and evaluation, and might further expand the application of SWA measurement to the early intervention of sleep disorders.

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1. Introduction

Sleep constitutes a fundamental behavioral mechanism for all living organisms. For humans in particular, there is increasing evidence that low quality sleep impairs physical health [1,2], cognitive function [3–7], recovery [8–12], memory [13–17], mood [18–20], and daytime functioning [21,22]. However, insomnia and non-restorative sleep are quite prevalent not only in patients with cognitive and psychiatric disorders, but also in the general population [23]. Scientific evaluation of sleep is crucial for people to recognize their sleep-related issues and seek effective interventions as soon as possible.

The examination of sleep from a scientific perspective started in the twentieth century. Further, a major advancement in sleep medicine, a discipline dedicated to the systematic study of the biology and disorders of sleep, was the discovery of the electrical activity of the brain [24]. With regard to the currently prevalent standard procedure in sleep-related studies, a routine overnight PSG requires multiple physiological channels and simultaneous recordings during sleep; EEG is the central indicator presently for the assessment of sleep. The most common quantification of sleep involves the stages defined as wake, rapid eye movement (REM) sleep, and non-REM (NREM) sleep. The R&K rules [25], introduced by Rechetschaffen and Kales almost five decades ago, classified NREM sleep into four stages, and the current American Academy of Sleep Medicine (AASM) rules [26] combined stages three and four and termed it as N3, also known as slow wave sleep (SWS).

However, since the time the sleep stages were first characterized, the requirement for the manual efforts necessary to score PSG and for the assessment of the basic architecture of sleep has remained relatively unchanged for several decades. Nowadays, concerns regarding the limitations of such procedures prevail in clinical practice. First, over-night attended monitoring with numerous electrodes [26], required by the standard complete PSG, often disturbs the natural sleep cycle of an individual and thus sleep-related assessments. Second, the quantification of sleep is rather arbitrary. Sleep depth, which is a continuous variable, is treated as though it alters in a stepwise fashion from light (stage 1), to intermediate (stage 2), to deep stage (SWS), leading to an inadequate description offered by the conventional R&K stages. Therefore, an adequate continuous measure of sleep depth is required. Third, conventional indices of sleep quality, such as sleep latency (SL), sleep efficiency (SE), and time assumed by different stages, are difficult to interpret. These difficulties are caused due to the wide range of values of these variables and the common contradictory changes observed across them when comparisons between two groups of patients are effected (or the same patients in two conditions) [23]. An integrated or alternative index is greatly required to furnish the description of the net difference in sleep quality between any two groups/interventions. Lastly, but no less significant, the visual scoring of PSG is commonly utilized in diagnosis but rarely for prompt sleep intervention. The analysis of sleep microstructure with the application of digital EEG analysis may provide a beneficial alternative to resolve these problems and effect a positive impact on practices in sleep medicine [23,27].

Furthermore, due to the complex and non-linear characteristics of EEG [28], non-linear approaches have been proposed to provide additional insights regarding the abundant dynamics of sleep [28,29]. Symbolic dynamics, which is based on the coarse-graining of the original signal, plays an essential role in the description of the evolution of non-linear systems [30]. Once the data obtained regarding a person's sleep dynamics has been transformed into a pattern whose elements merely comprise a few symbols (letters from some alphabet), the examination of the dynamics is simplified, reduced to the description of symbol sequences. However, in the process of symbolization, some amount of detailed information is lost, while certain invariant, robust properties of the dynamics may be retained or even emphasized [31–33]. Productive applications of symbolic methods are thus preferred in cases where robustness to noise is paramount [32].

Slow wave activity (SWA), presenting spectral power in the 0.75–4.5 Hz range, quantifies the dissipation of homeostatic sleep pressure during NREM sleep [34]. Now, SWA is commonly used as a quantitative measure of NREM sleep dynamics and an indicator of sleep depth or sleep intensity [35]; Olivier, Mathieu, Julie, Jacques, and Antonio (2010). To quantify SWA, fast Fourier transform (FFT) is an often used approach; however, FFT has intrinsic limitations to capturing underlying dynamics of the brain oscillations as they are nonlinear and non-stationary [36]. Drawing inspiration from the role of SWA in sleep evaluation and the advantage of the analysis based on symbolic dynamics, we introduced a symbolic analogue of SWA. Our aiming was twofold: one was to investigate whether this simple metrics can capture patterns of brain waves across different sleep stages and indicate potential biomarkers to assist the continuous measurement of sleep depth; and the other was to examine whether overall sleep quality is associated with EEG features observed during wakefulness or the first episodes of wake–sleep transition observed after light-off. Therefore, retrospective analysis was performed on EEGs derived from the PSG of 111 healthy adults, during different wake/sleep stages and different sections after light-off.

2. Methods

2.1. Overnight PSG recording and conventional indices of sleep quality

The overnight PSG obtained from the Sleep Heart Health Study-1 (SHHS-1) was utilized in this study. The SHHS entails a multi-center cohort study implemented by the National Heart Lung and Blood Institute to determine the cardiovascular and other heart-related consequences of sleep-disordered breathing. Unattended overnight PSG was performed with a portable PS-2 system (Compumedics, Abottsville, Australia). The requisite sensors were placed and the equipment was calibrated during an evening home visit by a certified technician. The data collection included C3/A2 and C4/A1 EEGs (Here, C3, A2, C4 and A1 are names of EEG electrodes which were placed according to International 10/20 System), right and left electrooculograms, a bipolar submental electromyogram, thoracic and abdominal excursions (inductive plethysmography

bands), airflow measures (detected by a nasal–oral thermocouple [Protec, Woodinville, WA]), finger pulse oximetry (Nonin, Minneapolis, MN) sampled at 1 Hz, electrocardiograms sampled at 125 Hz, body position (mercury gauge sensor), and ambient light (on/off, by a light sensor secured to the recording garment). After the retrieval of the equipment, the data was forwarded to a central reading center (Case Western Reserve University, Cleveland, OH) to perform the scoring according to a standard protocol. Finally, every 30-s epoch was scored [37]. The polysomnographic methods, scoring protocol, and quality assurance procedures adopted in this study have been previously described by earlier studies [37–39].

The conventional indices of sleep quality were calculated for each participant and included: total time in bed (TIB), defined as the time between light off and light on; total sleep time (TST), the time spent asleep between sleep onset and light on, wake after sleep onset (WASO), which refers to the total amount of time spent in wakefulness after falling asleep; the duration of each sleep stage, calculated as a percentage of TST. Other variables calculated included SE, SL, and REM latency (RL). SE was defined as the ratio of TST to TIB. SL was defined as the period starting from light off to the first three consecutive epochs of Stage 1 sleep or an epoch of any other stage. REM latency was defined as the period from sleep onset to the first epoch of REM sleep.

2.2. Subjects

One hundred and eleven healthy subjects were recruited in the study if they fulfilled the following inclusion criteria: (1) no habitual, daily alcohol intake; (2) no benzodiazepines or non-tricyclic antidepressants intake within two weeks of the SHHS1 visit; (3) no history of diabetes; (4) no history of stroke; (5) no hypertension status based on 2nd and 3rd blood pressure readings or treatment with antihypertensive drugs; (6) no self-reported hypertension; (7) no self-reported sinus trouble; (8) no coronary angioplasty, heart failure, heart attack, pace maker or stroke incidents; (9) Apnea–hypopnea Index (AHI), represented by the number of apnea and hypopnea events characterized by $\geq$ 3% oxygen desaturation per hour of sleep, of less than five ; (10) the entire recording was scored, and scoring started before light off and stopped after light on; (11) no more than 30 min of the sleep period yielded either lost or unscorable EEG, respiratory and oximetry data; (12) the value of SE is available and is not lower than 50%; (13) at least one epoch must be observed during each stage, i.e., wake, Stage 1 (S1), 2 (S2), SWS, and REM.

2.3. Symbolic dynamical analysis of EEG epochs

EEG signals from both derivations (C3/A2 and C4/A1) were imported into MATLAB for offline analysis. Each 30-s EEG epoch can be considered as a time series containing 3750 data points, expressed as $\{x_i: 1 \leq i \leq 3750\}$, since the original EEGs were sampled at 125 Hz. The EEG epoch was first normalized to a zero mean and unit standard deviation, and subsequently transformed into a series of words according to the following steps [40]:

(1) Sort the elements in the original series. Subsequently, with the alphabet size assumed as n, the quantiles, denoted as $\{t_i | i = 1, 2, \ldots, n-1\}$ in ascending order, are determined through the division of the sorted elements into n equal-sized parts, as depicted in Fig. 1. Subsequently, the symbolization can be fulfilled through Eq. (1) in the case of $n = 3$.

$$S_i = \left\{ \begin{array}{l} 0: x_i \leq t_1 \\ 1: t_1 < x_i \leq t_2 \\ 2: t_2 < x_i \end{array} \right\} (1 \leq i \leq 3750) \tag{1}$$

(2) Once the symbolic series is obtained, words that are constituted by successive symbols can be achieved through overlapping windows. The successive symbols in a window constitute a word, and the number of symbols in the window is termed as the word length. Assuming a normalized EEG epoch as an example, Fig. 1 indicates the way in which the equiprobable symbolization is developed.

It is worth noting that there are some special words that are constituted by identical symbols and thus termed as constant words. A nontrivially large percentage of constant words, denoted as P_{CW}, usually imply substantial low-frequency rhythms in the current symbolizing resolution of the original time series. Fig. 2 illustrates the original time series and their corresponding symbolic series of two EEG epochs in SWS and S1 respectively. As depicted in Fig. 2(A), the SWS epoch is characterized by a slowed oscillation and the emergence of a large-voltage low-oscillation waveform that results in a greater value of P_{CW} (47.8%, when the data length is set as 6) in comparison to that for S1 epoch (22.3%). Thus, the P_{CW} was proposed in the current study as a symbolic analogy of SWA.

For each subject, the computation of P_{CW} was processed for all scored 30-s epochs from light off to waking up in the morning. Different combinations of alphabet size (3, 4) and word length (3, 4, 5, 6) were utilized for the computation. For each EEG derivation, all the values of P_{CW} were subsequently combined for two separate analyses described below:

(1) Analysis 1: to average P_{CW} for each wake/sleep stage through the whole night, including all epochs from light off to waking up.

(2) Analysis 2: Regardless of the stages, to average P_{CW} for the first 15 min, 30 min, 60 min, and 90 min subsequent to the light off as well as for the whole night.

To further evaluate the relationship between sleep quality and symbolic dynamical features, indices of sleep quality were regressed with the averaged P_{CW} values for all 111 subjects in both analyses.

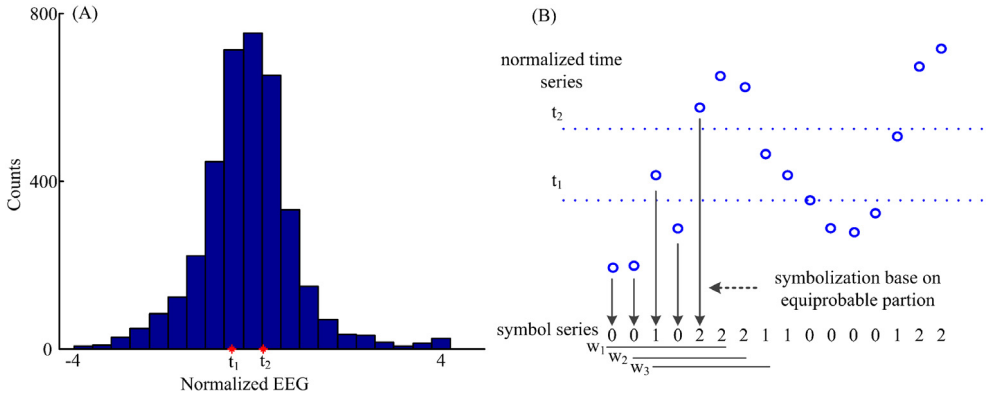

Fig. 1. (color online) Schematic diagram for the process of equiprobable symbolization. (A) The histogram of a normalized EEG time series, in which t_1, $t_2$correspond to the quartiles in the case of 3 symbols used. (B) Symbolizing the normalized time series and constructing words. A segment (16 successive data points, marked as blue circles) of the normalized time series are transformed into symbols based on the two quartiles (t_1 and t_2). By using overlapping windows (marked as horizontal solid-lines), three words, w_1, w_2 and w_3, are obtained. The word length used here is 6.

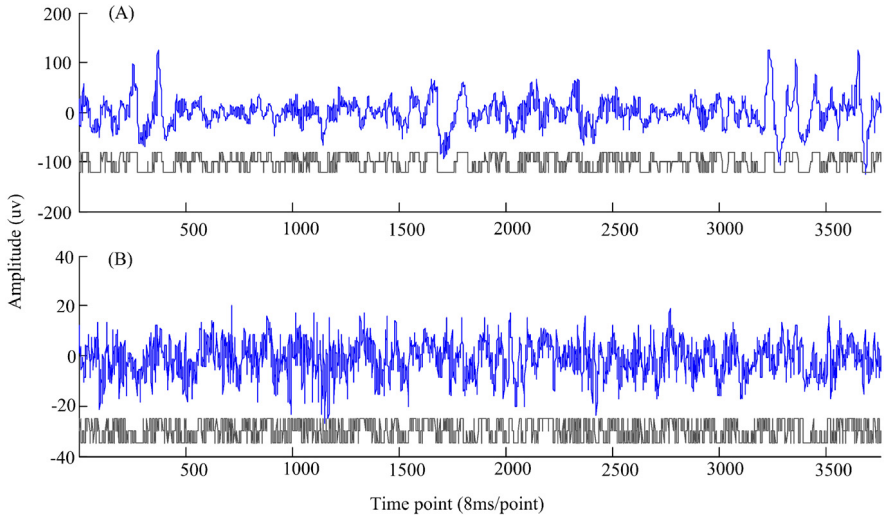

Fig. 2. (color online) EEG epochs and their corresponding symbolic series at different sleep stages (A for SWS and B for S1) are illustrated. The alphabet size used in the equiprobable symbolization is set as 3.

2.4. Statistical analyses

Statistical analyses were performed with the application of MATLAB (Mathworks Inc., Natick, MA). The relationship between the averaged P_{CW} and the demographical indices, i.e., age, height, weight, and body mass index (BMI), was examined by a partial correlation analysis. The partial correlation analysis was further applied for the evaluation of the relationship between averaged P_{CW} and indices of sleep quality, while controlling for the demographical characters. Furthermore, due to the loss of homogeneity (Bartlett's test, $p < 0.05$), Friedman's non-parametric analysis of variance (ANOVA) was utilized for the averaged P_{CW} among five wake/sleep stages in Analysis 1, and a post hoc analysis was conducted with two-sample Wilcoxon sign rank tests with Tukey–Kramer adjustment.

3. Results

The results derived from both EEG derivations are similar; therefore, only the results obtained from C3/A2 derivation are presented in this study. The following results are based on an equiprobable symbolization with the alphabet size three and word length six, as the results exhibited a slight alteration when different combinations of alphabet size (3, 4) and word length (3, 4, 5, 6) were applied.

Table 1
Demographics and indexes of sleep quality.

Gender	20M/91F
Age (years)	56 [48.5, 66]
Height (cm)	162.6 [157.6, 167.8]
Weight (kg)	68.2 ± 11.4
Body Mass Index (kg/m^2)	25.6 ± 4.0
Time in bed (min)	437.1 ± 60.5
Total sleep time (min)	369.2 ± 60.3
Wake after sleep onset (min)	33 [19.8, 62]
Time in Stage 1 as a % of TST	3.9 [2.6, 5.2]
Time in Stage 2 as a % of TST	54.6 ± 10.8
Time in SWS as a % of TST	20.7 ± 11.7
Time in REM as a % of TST	21.6 [16.7, 24.3]
Sleep efficiency (%)	86.6 [79.0, 91.9]
Sleep latency (min)	18.5 [8, 31.8]
REM latency (min)	69.5 [57.5, 90.5]

Note: If the data violate the normality, values are expressed as median [lower quartile, upper quartile], otherwise as mean ± SD. Abbreviations: SWS: slow wave sleep; TST: total sleep time; REM: rapid eye movement.

Table 2
Correlation coefficients of demographics and average P_{CW}.

	Analysis 1					Analysis 2				
	WAKE	S1	S2	SWS	REM	15 min	30 min	60 min	90 min	ALL
Gender	−.16	−.13	−.18	−.04	−.17	−.1	−.08	−.12	−.09	−.1
Age	−.17	−.05	−.01	−.01	−.16	−.08	−.08	−.1	−.1	−.08
Height	.09	.07	.02	.04	.02	.04	−.01	−.03	−.03	−.01
Weight	−.12	−.11	−.04	−.04	−.03	−.07	−.03	−.02	−.004	−.01
BMI	.15	.13	.06	.06	.03	.09	.04	.02	.02	.03

Note: Abbreviations: P_{CW}: percentage of constant words; WAKE: wakeful stage; S1: Stage 1; S2: Stage 2; SWS: slow wave sleep; ALL: the whole night from light-off to waking-up; BMI: Body Mass Index. No significant correlation was found between any P_{CW} outcome and demographic characters.

3.1. Demographics and indices of sleep quality

One hundred and eleven healthy subjects (20 males and 91 females) were included in the final analysis (Table 1). The sample had a median age of 56 years and mean BMI of 25.6 ± 4.0 kg/m^2. With regard to the BMI, a majority of the participants were identified as normal (18.5–25 kg/m^2) or overweight (25–30 kg/m^2), and all subjects showed an AHI value lower than 5 events/hour. The standard PSG scoring results revealed that the mean TST was 369.2 min, and median SE and SL were 86.6% and 18.5 min, respectively. The ratios of scored sleep stages, S1, S2, SWS, and REM sleep, were approximately 4%, 55%, 21%, and 20% respectively, results consistent with the general sleep architecture in adults [41]. As illustrated by Table 2 , no significant correlation could be determined between P_{CW} outcomes and demographic characters of the sample, including age, gender, height, weight and BMI.

3.2. Results of analysis 1: P_{CW} for each stage

Fig. 3 illustrates the average P_{CW} across all epochs scored in each of the conventional stages in individual patients. The values of P_{CW} were observed to be associated with wake/sleep stages. For the NREM sleep stage, the average P_{CW} exhibited progressive increase from S1 to SWS. As depicted in Fig. 3(C), a main effect of stage on the average P_{CW} was determined through ANOVA; further, significant differences among all stage pairs (post hoc comparisons, $p \leq 0.001$), except for wake and S1 were observed.

For any sleep stage, no significant correlation was discovered between the average P_{CW} and the conventional indices of sleep quality in most cases (Table 3, Analysis 1). However, significant correlation was discovered between the average P_{CW} in wake and TST, WASO, SE, as well as SL (Table 3, Analysis 1). Furthermore, a lower value of P_{CW} in wake stage corresponds to reduced SE and TST as well as prolonged SL and WASO, indicating a worse sleep quality during night.

3.3. Results of analysis 2: P_{CW} of different time duration since light off

As illustrated in Table 3, regardless of the wake/sleep stages, the averaged P_{CW} values of EEG epochs exhibit a correlation with various indices of sleep quality derived from overnight PSG scoring, even when 15-min recordings of EEG immediately after light off were utilized. As exhibited by in Table 3 (Analysis 2), a negative correlation between SE and the average P_{CW} in 15-min EEG recordings shows significance. Further, the average P_{CW} exhibits a significant correlation with SL. When longer time duration (e.g. 30 min after light off) was utilized for P_{CW} computation, an increased amount of indices of sleep quality

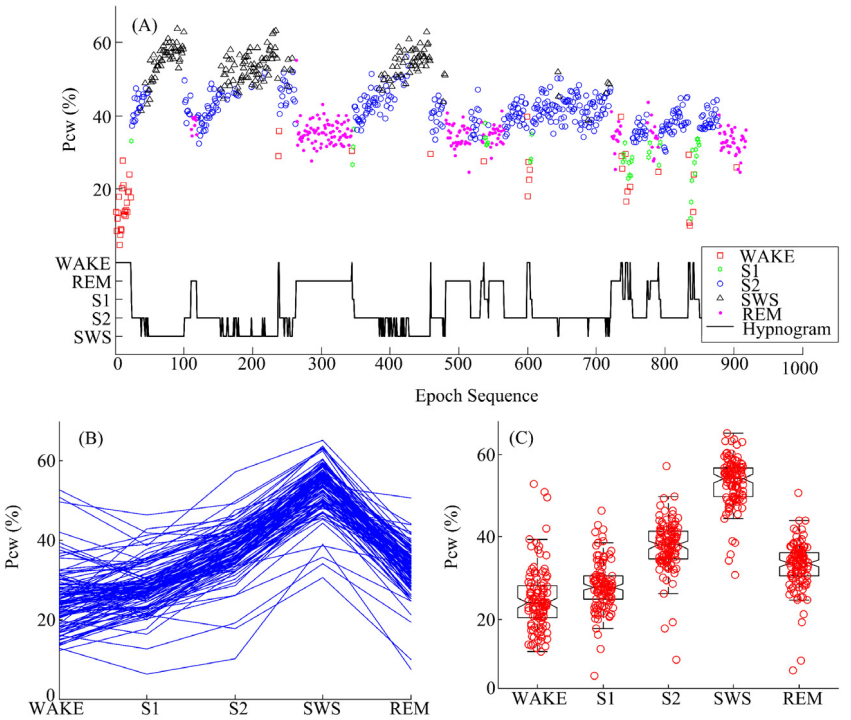

Fig. 3. (color online) P_{CW} in each wake/sleep stage over the whole night for all the subjects. (A) A Hypnogram and typical scatter of P_{CW} along with the sequence of 30-s epochs obtain from a female subject, 64 years old with a BMI of 23.5; (B) plot of average P_{CW} in each wake/sleep stage for each subject; (C) scatter — boxplot for the averaged P_{CW} in each wake/sleep stage for all the subjects. ANOVA suggests that stage has a significant main effect on the value of P_{CW} ($\chi^2 = 371.32$, $p \ll 0.001$), and post-hoc comparisons show that there is significant difference between each two stages ($p \ll 0.001$), except for between WAKE and S1 ($p > 0.05$). Abbreviations: P_{CW}: percentage of constant words; WAKE: wakeful state; REM: rapid eye movement sleep; S1: Stage 1; S2: Stage 2; SWS: slow wave sleep.

Table 3
Correlation coefficient between indexes of sleep quality and P_{CW}.

	Analysis 1					Analysis 2				
	WAKE	S1	S2	SWS	REM	15 min	30 min	60 min	90 min	ALL
TIB	−.08	−.01	.03	.07	.04	−.11	−.18	−.13	−.13	−.07
TST	.21*	.11	.13	.01	.13	.13	.19*	.29**	.28**	.22*
WASO	−.31*	−.24*	−.19*	.06	−.15	−.19	−.26**	−.24*	−.22*	−.39**
TS1%	.07	.05	−.01	.07	−.08	.16	.07	−.04	−.05	−.14
TS2%	−.08	−.10	−.09	.05	−.24*	−.15	−.19*	−.19*	−.15	−.32**
TSWS%	.04	.03	.07	−.09	.18	.10	.14	.14	.10	.32**
TREM%	.04	.10	.03	.05	.11	−.00	.05	.09	.10	.02
SE	.43**	.19	.15	−.08	.14	.35**	.54**	.63**	.61**	.44**
SL	−.30*	.06	.04	.06	−.01	−.35**	−.57**	−.75**	−.73**	−.18
RL	−.09	−.14	−.06	−.06	−.07	−.17	−.30**	−.29**	−.26**	−.12

Abbreviations: P_{CW}: percentage of constant words; WAKE: wakeful state; S1: Stage 1; S2: Stage 2; SWS: slow wave sleep; REM: rapid eye movement sleep; ALL: the whole night from light out to waking up; TIB, total time in bed; TST, total sleep time; WASO, wake after sleep onset; TS1%, percentage of time in Stage 1; TS2%, percentage of time in Stage 2; TSWS%, percentage of time in SWS; TREM%, percentage of time in REM; SE, sleep efficiency; SL, sleep latency; RL, REM latency.

*Represents the correlation $p < .05$.

**Represents $p < .01$.

exhibited significant correlation with P_{CW}. As presented in Table 3 and Fig. 4, lower average P_{CW} for limited time (30–60 min) EEG recordings correspond to reduce TST and SE as well as more time spent on wakeful state and Stage 2. Furthermore, a significant correlation was discovered between P_{CW} and SL as well as RL. All these results suggest that a decline in sleep quality during the whole night may be evaluated through the application of limited time (15–60 min) EEG recordings.

Furthermore, significant correlations were determined between the average P_{CW} across the whole night and TST, WASO, time in Stage 2, time in SWS, and SE (Table 3, Analysis 2). A lower average P_{CW} over the whole night corresponds to a reduced TST, time in SWS and SE, as well as an increased amount of time spent on wakeful state and Stage 2; it further suggests a decline in sleep quality during the night.

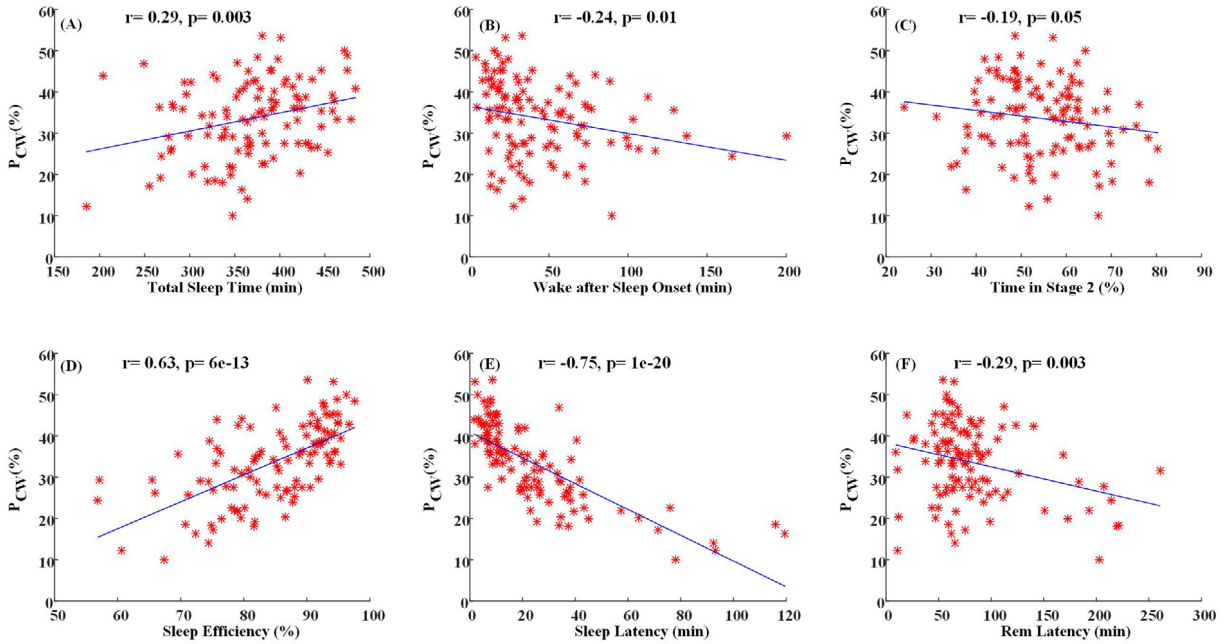

Fig. 4. (color online) Scatter plot of average value of P_{CW} in 60 min after light off, in regardless of wake/sleep stages, as a function of the indices of sleep quality. The correlation coefficient (r-value) as well the p -value between indexes of sleep quality and P_{CW} were also marked in subplot respectively. The blue line in each subplot represents the first-degree polynomial fitted curve. Abbreviations: P_{CW}: Percentage of constant words; REM: rapid eye movement.

4. Discussion

In this paper, we aimed to measure the sleep depth and evaluate the overall sleep quality through the analysis of a single-channel EEG based on symbolic dynamics. The percentage of constant words observed in the symbolic sequence, denoted as P_{CW} in this paper, was proposed as an objective measure for sleep depth and sleep quality. The key findings are as follows: (1) P_{CW} exhibits significant difference across the wake/sleep stages; it especially increases gradually when the sleep becomes deeper, indicating its potential as a biomarker for the continuous measurement of sleep depth; (2) The averaged P_{CW} values of EEG epochs during wakeful state exhibit a correlation with some traditional indices of sleep quality, such as total sleep time, time spent on wake after sleep onset, sleep efficiency, and sleep latency, while the P_{CW} values during sleep yield limited or no correlation with those indices; (3) Moderate to high levels of correlations exist between the traditional indices of sleep quality and average P_{CW} of EEG epochs for limited time duration, even 30 min after light off, suggesting P_{CW}'s possible application as an alternative indicator of the overall sleep quality as well as an indicator for timely sleep intervention.

PSG constitutes the cornerstone of investigations in clinical sleep medicine; however, the interpretation of sleep in these studies continues to depend almost exclusively on visual scoring that applies the R&K rules proposed nearly 50 years ago. In a recent review in sleep science and practice [23], Younes presented the prevailing doubts about the validity of R&K's N1 to N3 stages as a measure of sleep depth, due to the commonplace inter-rater variability in scoring sleep. He clearly advocated the inclusion of digital scoring in routine PSG analyses, a practice that can extract additional information inaccessible through visual scoring. The results in the present work support the view that the application of metrics derived from the digital analysis of EEG will provide a propitious technique to evaluate sleep depth and positively impact sleep medicine practice. Furthermore, the significant correlations observed between the proposed metric, P_{CW}, and various indices of sleep quality supports the application of the digital EEG analysis as the next generation tool for the objective evaluation of sleep quality that does not necessitate arduous interventions during visual PSG scoring.

Additionally, correlations between average P_{CW} and various indices of sleep quality were preserved when the proposed approach was applied to EEGs for short sections (15–90 min). With prolonged sections, the correlations gradually increased, for 30 or 60 min, while they exhibited a decrease in relation to a 90-min section, suggesting that a longer period of monitoring may not be necessary for sleep assessment. In fact, the analysis based on EEGs in 30 min already demonstrated moderate correlations between P_{CW} and overall sleep quality. Additional analysis that employed the EEG before sleep onset (different data lengths for each participant) yielded no better results than the outcomes presented previously, indicating that specified data acquisition is not necessary.

These findings may be utilized to indicate whether an intervention is required for the night. For example, insomnia and hypnotic use are highly prevalent in the current practice [42–44]. Although multiple interventions are currently available, the indication of the effectiveness of its application prior to the night is uncertain. In fact, most people with insomnia

complain about being unable to fall asleep because they cannot switch off their "racing" mind [45–47]. A study also found that under high mental load the urgency to fall asleep increased sleep onset latency [48]. In addition, pre-sleep arousal has been approved to mediate the relationship between daily stress and subjective sleep quality [49]. Existing evidence suggests that the manipulation of pre-sleep cognitive activity leads to changes in sleep onset latency [48,50,51]. Through the integration of the approach proposed in this study, the efficacy of sleep interventions [52], such as the cognitive behavioral therapy for insomnia (CBT-I), could be evaluated through a short-term EEG recording accomplished through a wearable EEG device during sleep initiation. In addition, P_{CW} may serve as a potential indicator to provide clue for the effectiveness of early sleep intervention. Clinicians acknowledge that interventions for sleep improvement can be challenging, particularly when it comes to the intervention customization to individuals. By the approaches proposed in this study, training, hypnotic medication, or non-pharmacological interventions such as CBT-I, mindfulness-based therapy, or music therapy, can be quantified and evaluated by a short time EEG recording. Thus, specific interventions can be customized to insomniac subjects in need, and the efficacy can be easily tracked using EEG at early time after light off. By such techniques, clinicians may get clear evidence on populations who benefit from a certain practice, and clear clue to adjust the "dosage" of intervention without the disturbance of wearing multiple sensors and wires over the night. Further investigations of the clinical application of this approach on those populations are warranted in future studies. Moreover, due to the essential role of wakeful state in relation to the overall sleep quality, pre-sleep status may provide relevant insight regarding the clinical understanding of the human sleep mechanism, and thus demands further investigations. Future studies are encouraged to exam whether the dynamics (e.g. complexity) of brain waves at pre-sleep status or during sleep latency is associated with sleep drive or sleep quality over the night.

Finally, regarding the used symbolic approach, we made some more considerations. Firstly, as noise-assistance is a main advantage of symbolic analysis [32,53], we tested the performance of the current method when Gaussian noise with different powers were added to the original EEG signals noise. Secondly, we calculated two more symbolic parameters, the percentage of forbidden words and the Shannon Entropy of words. Forbidden words is a kind of words which never occur in the distribution of words in the current symbolization scheme whereas Shannon entropy was used to describe the distribution of all occurring words. Thirdly, an ordinal coding scheme [54] was used instead of the equiprobable symbolization and the Shannon Entropy of words was computed as there is no constant words within an ordinal coding framework. The results were shown in Fig .5. As demonstrated in Fig. 5(A), the proposed metric is robust in differentiating NREM sleep when a noise with equal power was mixed, supporting the use of symbolic dynamic analysis in a noisy circumstance. Fig. 5(B) and Fig. 5(C) shows almost similar results with the proposed metrics, indicating a limited promotion by a comprehensive consideration of all words as replacements for constant words. Finally, as shown in Fig. 5(D), a more clear overlap of the boxplots among stages can be observed than that in Fig. 3(C). Compared with the proposed method, the ordinal coding scheme should focus more on the fast-changing components in the original signal. Therefore, the results shown in Fig. 5(B)-(D) further support the importance of SWA measuring in sleep evaluation.

In conclusion, the proposed method demonstrated its potential value in sleep medicine practice. Provided the statistical insignificance of P_{CW} values between wake and S1, two strategies can be employed in future studies to distinguish the two stages. One involves the inclusion of additional physiological signals, such as electromyogram and electrooculograms, and another entails the improvement of the data processing methods. Due to the equiprobable symbolization, the probability of each symbol in the alphabet becomes uniform on the original time scale, and the frequency of each probable word depends solely on the time structure of the original series. Therefore, the dynamic features of the original series can be directly reflected through the distribution of different words. However, the amplitude information pertaining to each stage was lost [40]. Further promising results might be attained through the combination of other approaches that can characterize the amplitude of EEG.

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Conflict of interest

None.

Ethical approval

The study protocol of SHHS was approved by the institutional review board of each participating center, and each participant signed informed consent. All methods were carried out in accordance with relevant guidelines and regulations. The current study only analyzed de-identified data from the SHHS database, and did not involve a research protocol requiring approval by the relevant institutional review board or ethics committee.

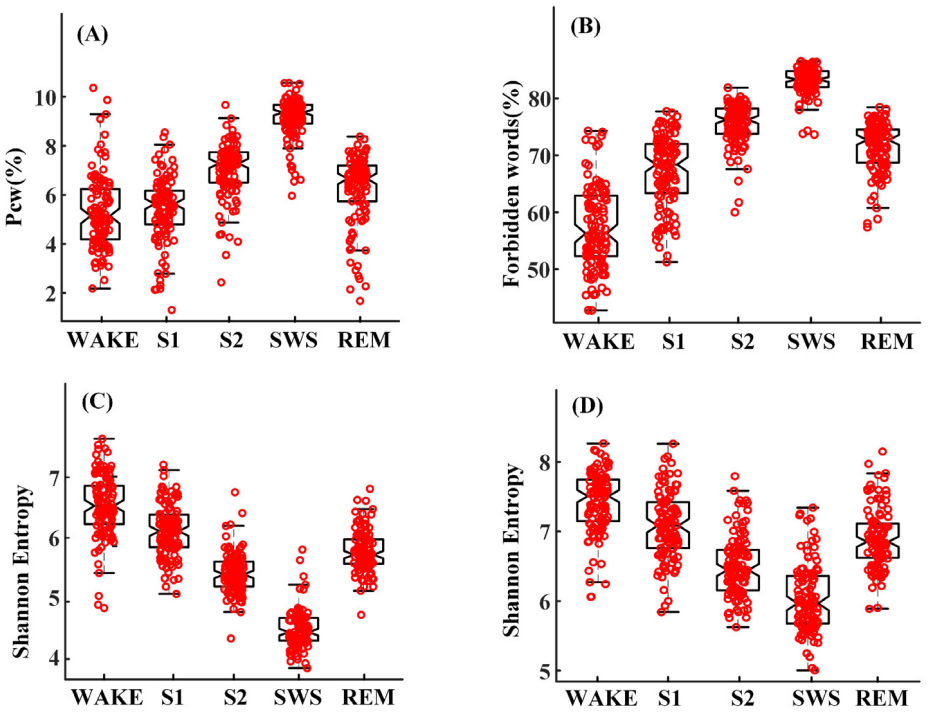

Fig. 5. (color online) Scatter — boxplot for the averaged symbolic measures in each wake/sleep stage for all the subjects. (A) P_{CW} values (alphabet size was set as 3 and word length was set as 6) when equal — power white noise was added to the original signal; (B) the percentage of forbidden words in the case of equiprobable symbolization with alphabet size 3 and word length 6; (C) the Shannon Entropy of words in the case of equiprobable symbolization with alphabet size 3 and word length 6; (D) the Shannon Entropy of words in the case of ordinal coding with word length 6. Abbreviations: P_{CW}: percentage of constant words; WAKE: wakeful state; REM: rapid eye movement sleep; S1: Stage 1; S2: Stage 2; SWS: slow wave sleep.

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