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EEG recurrence markers and sleep quality

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ABSTRACT

Objectives: To show that EEG markers formed using the variable *percent recurrence* reliably quantified two related aspects of sleep quality, sleep depth and sleep fragmentation. As hypotheses, the depth marker would increase and the fragmentation marker decrease in patients where improved sleep quality occurred when assessed by polysomnography.
Methods: The patients (N = 20) had been diagnosed with obstructive sleep apnea during diagnostic polysomnography (dPSG), and had exhibited increased REM sleep (clinical indication of improved sleep quality) during subsequent polysomnography to titrate the pressure of a treatment device (cPSG). Percent recurrence was computed second-by-second from the EEG; sleep-depth and sleep-stability markers were obtained algorithmically. By assumption, the markers contained temporal information regarding the extent of deterministic (non-random) brain activity. Marker means were compared between the dPSG and the cPSG for NREM and REM sleep.
Results: Sleep depth was greater and sleep fragmentation was less during cPSG, as hypothesized ($P < 0.05$). The effects occurred during NREM and REM sleep, but were greater during NREM sleep ($P < 0.05$). At least one of the predicted changes occurred in 95% of the patients.
Conclusions: The factors generally regarded as responsible for subjective sleep quality were objectively quantified on the basis of dynamical changes in the EEG.

1. Introduction

Human sleep and associated events are assessed on the basis of rules applied to simultaneously recorded physiological signals [1]. Three stages (N1, N2, N3) and particular arousal events (abrupt changes) are identified from the electroencephalogram (EEG), and a fourth stage (REM) is identified from the coordinated behavior of several signals including the EEG. The N3 stage is commonly regarded as deep sleep. The depth of sleep together with the rate of arousal events are determinants of sleep quality [2]. Loss of sleep depth and/or increases in arousal events produce non-restorative sleep, and are associated with various sleep disorders including obstructive sleep apnea (OSA).

Present methods for measuring the depth of sleep are problematical [3–7]. Determining the intensity of stimuli needed to wake a subject has been used to quantify sleep depth [3,4], but that method variably classified REM as the deepest level of sleep [5], intermittently deep [6], or as similar in depth to N1 and N2 sleep [6], depending on how the threshold was measured. Delta power is a marker for sleep depth during non-REM (NREM) sleep [7], but no equivalent marker exists for REM sleep. Similarly, additional refinement of scoring arousals is needed [8]. We recently showed that a recurrence marker computed by algorithmic analysis of the EEG stratified all sleep stages, increased progressively with NREM sleep-stage depth (N1 < N2 < N3), and characterized sleep fragmentation caused by arousal events [9].

REM rebound (an increase in percent of overnight sleep that is staged as REM) occurs during recovery from chronic stress, including restorative sleep following sleep deprivation [10] and initiation of treatment for OSA using continuous positive airway pressure (CPAP) [11–14]. CPAP-associated REM rebound (CARR) is generally accepted to indicate deeper and less fragmented sleep [11–14]. We therefore expected an increase in recurrence in CARR patients and a decrease in the variability of the recurrence, compared with the corresponding values determined prior to initiation of CPAP.

Our goal was to evaluate the capability of the EEG-based recurrence variable *percent recurrence* to quantify sleep depth and sleep fragmentation. The first aim was to show that a recurrence depth marker increased in patients who experienced CARR (increased sleep depth). The second aim was to show in the same patients that a recurrence fragmentation marker exhibited a decreased rate of change (decreased sleep fragmentation).

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2. Methods

2.1. Subjects

We reviewed consecutive records of patients who underwent attended overnight diagnostic polysomnography (dPSG) that was positive for OSA (apnea–hypopnea index (AHI) ≥5 events/hr), and who subsequently underwent overnight CPAP-titration polysomnography (cPSG) during which CARR (clinical indicator of increased sleep depth and improved sleep quality) was observed. CARR was defined as an increase in REM as a percentage of total sleep time of at least 20%. This threshold was higher than that used previously [11–14], but sufficiently low to ensure that an adequate number of patients were available for study after screening the database (>500 studies). Exclusion criteria included <30 minutes of REM sleep in any study, significant medical co-morbidities, current use of sleep-altering medications, and prior treatment for OSA. The study group consisted of the first 20 consecutive patients who met all the study criteria; the selected patients exhibited quite severe OSA (Table 1). Although CPAP treatment markedly reduced the AHI (clinical indicator of reduced sleep fragmentation), the patients still exhibited OSA (Table 1). The PSGs were staged by consensus between two sleep-medicine physicians, using standard rules [1], resulting in the assignment of every 30-sec epoch of the PSGs into one of five stages: REM, N1, N2, N3, or wakefulness after sleep onset (WASO). For purposes of simplifying the subsequent analysis (see below), the N1, N2, and N3 stages were combined into the NREM stage.

To estimate the recurrence values computed during wakefulness from EEGs of healthy individuals, eyes-closed vigilant EEGs were recorded from 20 clinically normal subjects. They were selected as a representative normal sample (median age 34 years, half of each gender), not as age and gender matches for the patients. The EEGs were analyzed similarly to those from the patients (see below). All experimental procedures were approved by the institutional review board for human research.

2.2. EEG measurements

PSGs (which included 6 EEGs) were recorded with commercial equipment (Respironics, Alice 5, Murrysville, PA, USA), using standard digital specifications and electrode montage (O1, O2, C3, C4, F3, F4, International 10–20 system) [15]. The EEGs were digitized at 500 Hz, and exported as CSV files for analysis.

Vigilant EEGs from normal subjects were recorded for 10 minutes in a dark isolation chamber (assumed reasonably sufficient for estimating normality) to mitigate the effect of irrelevant or random ambient stimuli. The electrode montage used (O1, O2, C3, C4, P3, P4, referenced to linked ears) was chosen in accordance with the standard practice for recording EEGs in our research laboratory. The EEGs were digitized at 500 Hz, and stored as ASCII files for analysis. The recurrence values were averaged over all electrodes and all subjects to provide estimates of recurrence and its variability in normal awake subjects (the cognitive state where the variables have their extreme values).

Table 1
Characteristics of the sleep patients. BMI, body mass index. AHI, apnea–hypopnea index. dPSG, diagnostic polysomnogram. cPSG, CPAP polysomnogram. (Mean ± SE).

Number of patients	20
Age (years)	46.5 ± 3.1
BMI (kg/m^2)	47.4 ± 2.0
Male/Female (%)	67/33
AHI (events/hr)	100.6 ± 6.1 (dPSG) 16.1 ± 3.1 (cPSG)

2.3. Recurrence analysis

All EEGs were digitally filtered to pass 0.5–35 Hz and evaluated using recurrence analysis in a standard numerical computing environment (Matlab, Mathworks, Natick, MA, USA). The signal-processing techniques were developed to study nonlinear physical systems and subsequently extended to physiological signals [16,17], including the vigilant and sleep EEGs [9,18–20]. Briefly, at time t a 5-component vector was formed that consisted of the EEG amplitude at t and four earlier times identified by four successive lags of five points (10 msec). The next vector in the sequence was at $t + 10$ msec and consisted of the EEG at that time, t, and the values 10, 20, and 30 msec earlier. The sequence of all such vectors obtainable from 1 sec of the EEG (480 vectors, given our choices of sampling rate, vector dimension, and number of lag points) formed a path (in a mathematical space) that is conventionally interpreted to be a result of the deterministic (non-random) activity in the EEG. By hypothesis, the EEG determinism increased and its variability decreased as a consequence of CPAP treatment.

The determinism was quantified second by second using the recurrence variable *percent recurrence* (r), defined as the percent of the 480 vectors in the path that were near other vectors [17]. The Euclidean norm was used for measuring distance, and vectors were identified as *near* if they were within 15% of the distance between the two vectors that were furthest apart. These choices (and those for dimension and lag) were previously found to be useful for quantifying deterministic activity in the EEG [9,18,19].

Approximately 60 sec × 60 min × 8 hrs = 28,800 values of r were computed for a typical eight-hour overnight EEG, resulting in the time series r(t). For the vigilant subjects, 60 sec × 10 min × 6 derivations × 20 subjects = 72,000 r values were averaged to obtain the mean value of recurrence in normal subjects during wakefulness ($\bar{r}$).

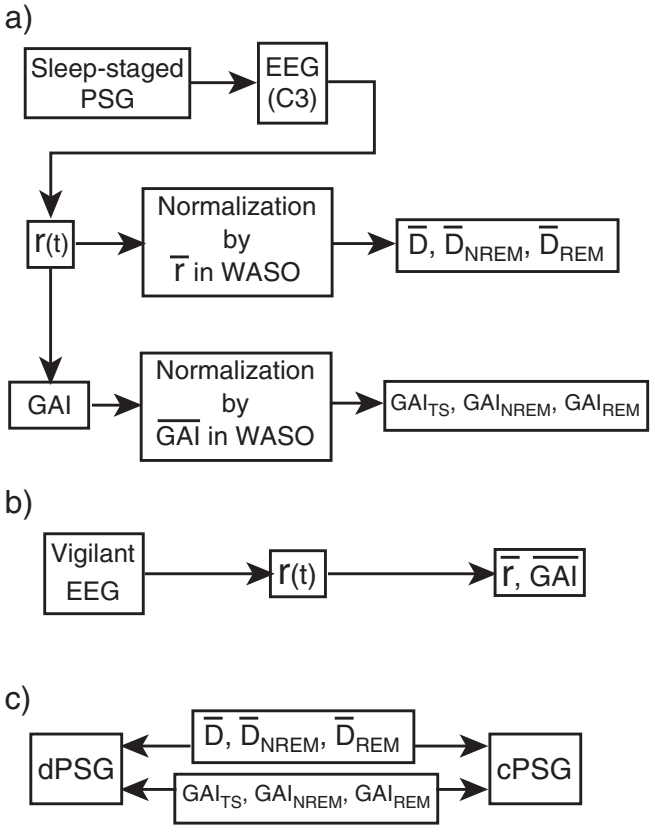

Fig. 1. Experimental design. a) Computation of recurrence markers from overnight sleep EEGs. b) Computation of recurrence markers from vigilant EEGs. c) Statistical design.